

FIG. 1



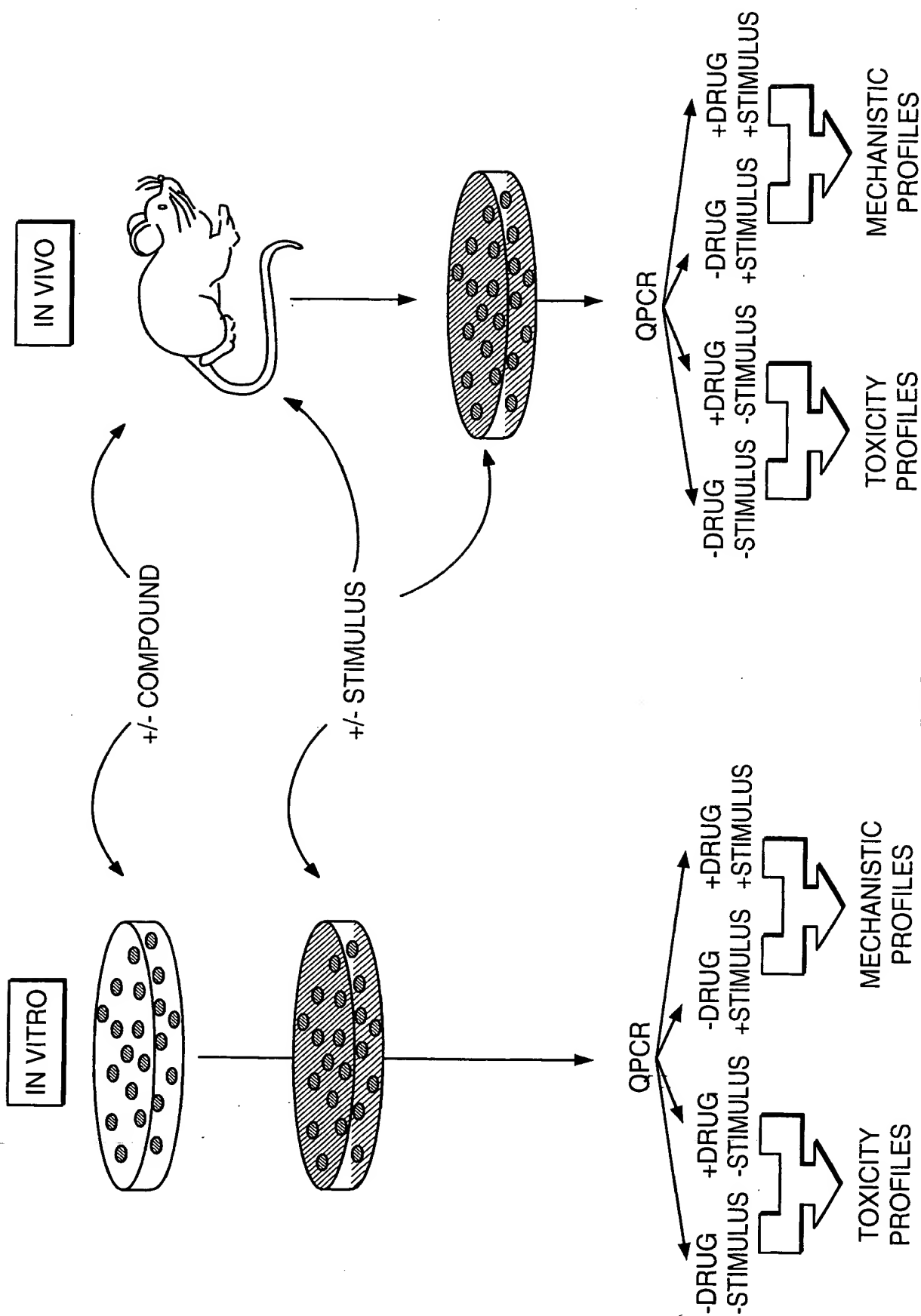


FIG. 3

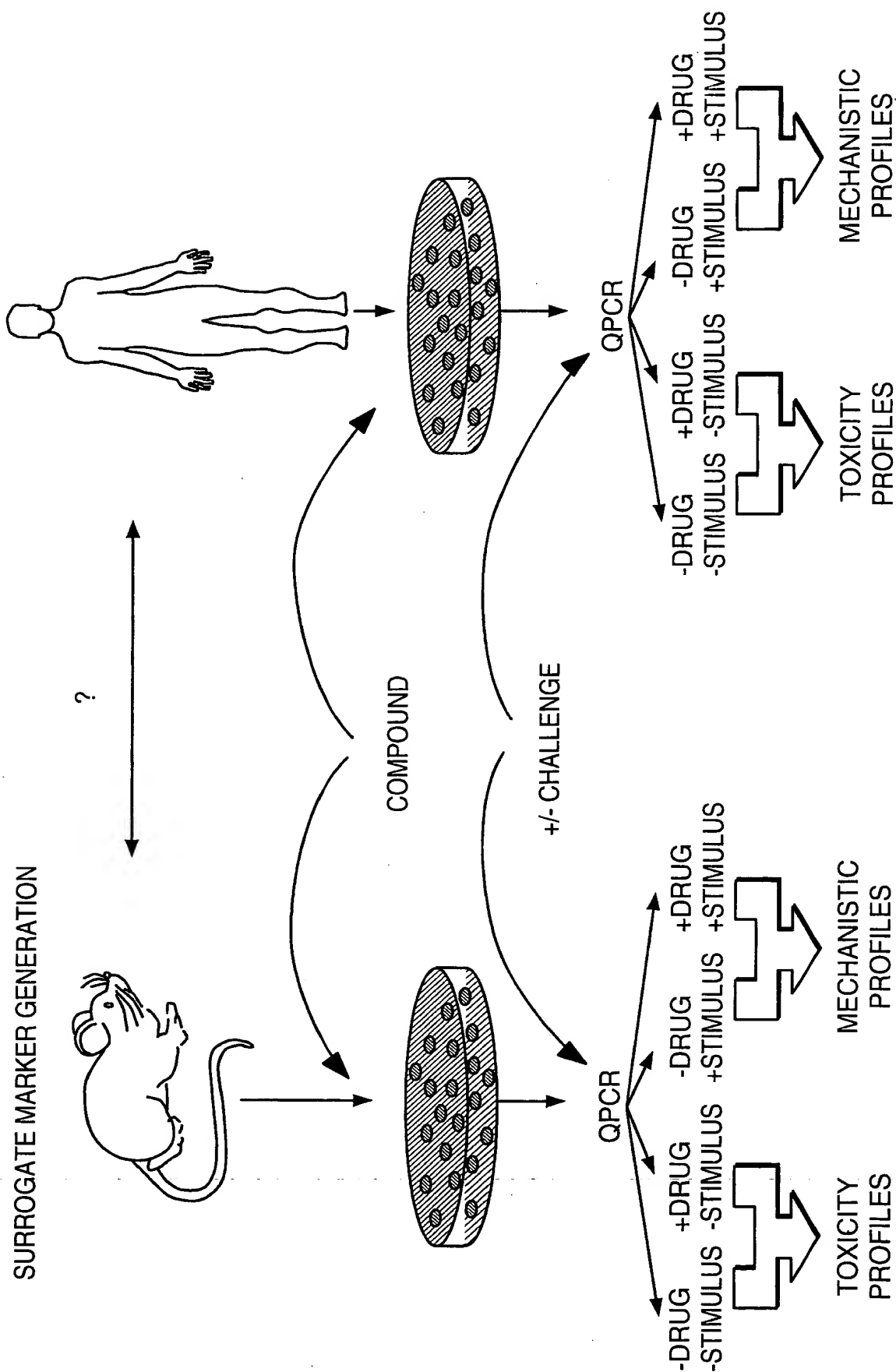
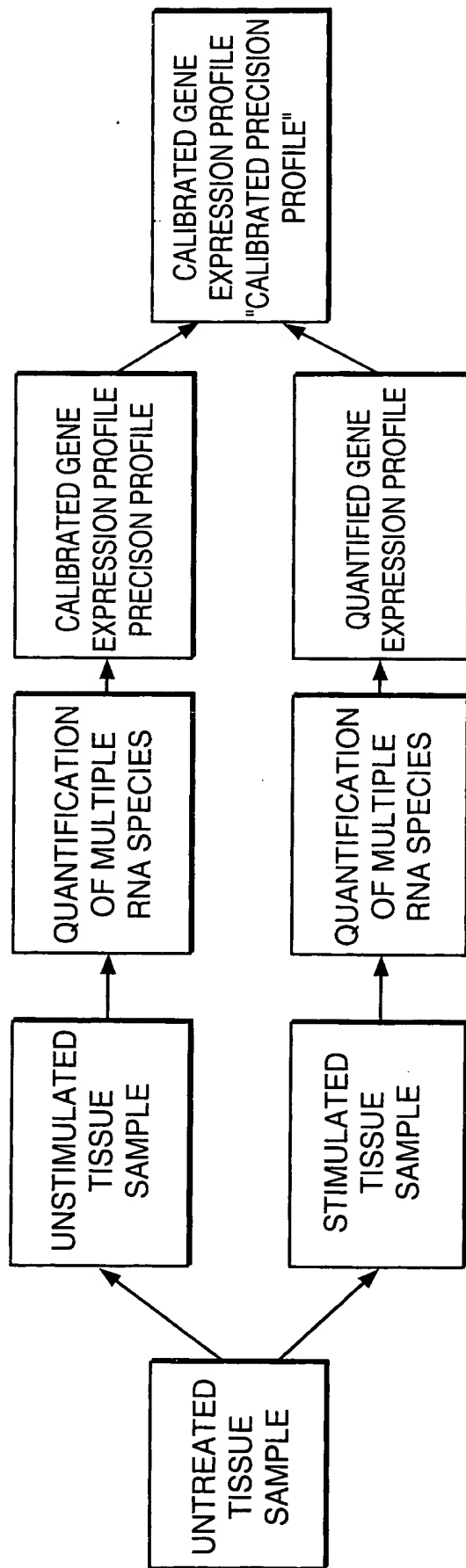


FIG. 4

PRODUCING A "CALIBRATED PRECISION PROFILE"



SOURCE PRECISION MEDICINE

FIG. 5



[illegible]

**FIG. 7**

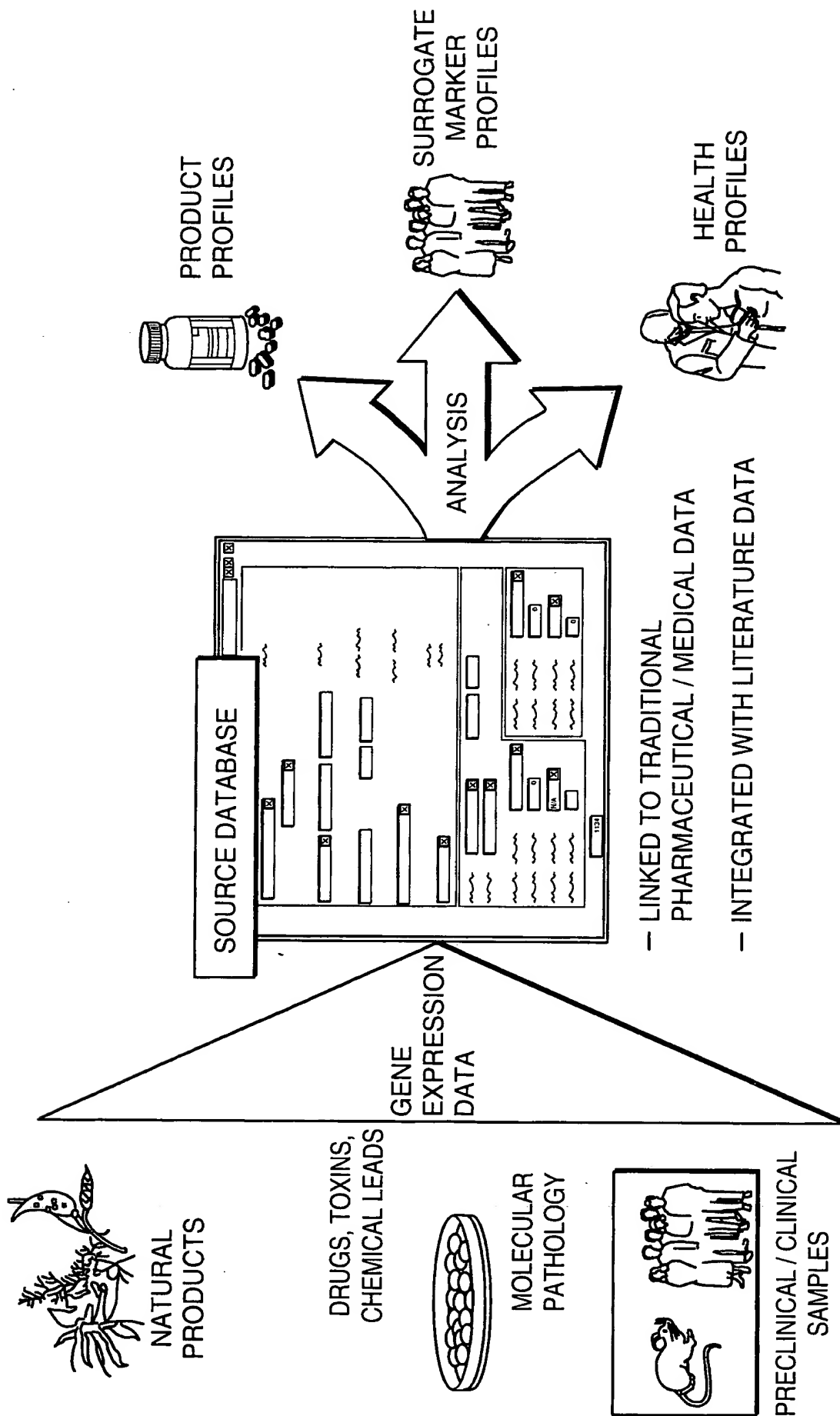


FIG. 8



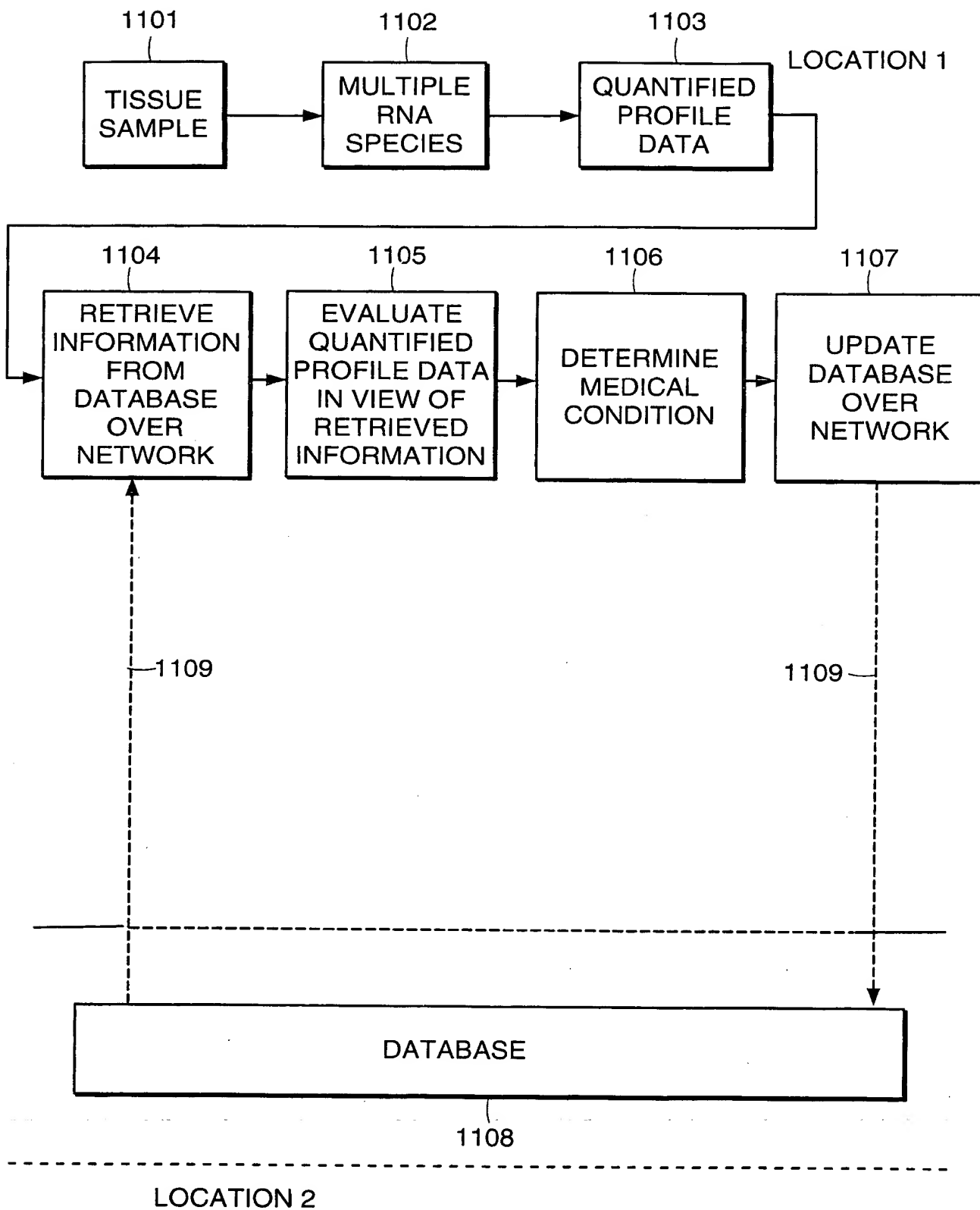
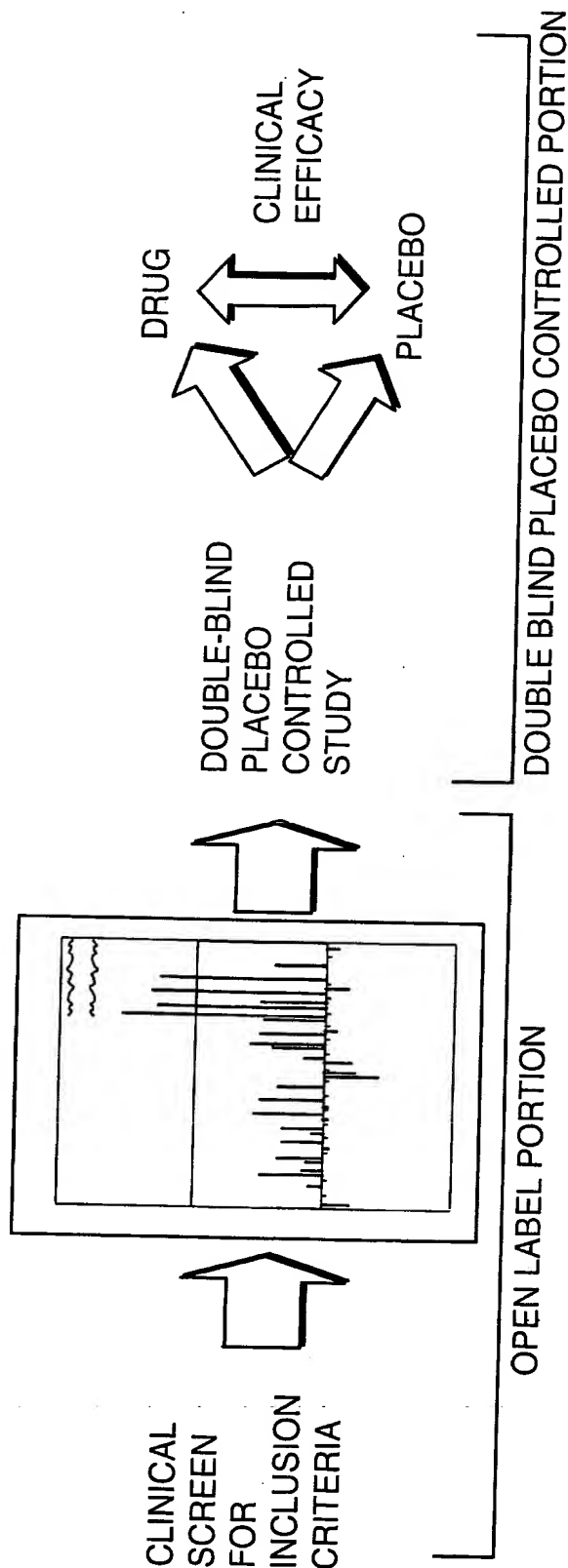


FIG. 9

# PHASE TWO CLINICAL TRIAL DESIGN USING PRECISION PROFILING



-THE TARGET CLINICAL POPULATION CAN BE EVALUATED FOR RESPONSIVENESS TO THERAPY BY FOCUSING ON DRUG RESPONSE GENE PROFILING

-"SIGNAL TO NOISE" CAN BE ENHANCED BY REMOVING NON-RESPONDERS FROM THE SECOND PORTION OF THE STUDY

-DOSE CAN BE OPTIMIZED ON AN INDIVIDUAL BASIS TO MAXIMIZE THE IMPACT ON THERAPEUTIC OUTCOME

- CLINICAL RESPONSE/NON-RESPONSE CAN BE CORRELATED WITH DISEASE RESPONSE GENE PROFILING

- CLINICAL EFFICACY CAN BE MEASURED WITH GREATER PRECISION

- FUTURE STUDIES CAN BE PLANNED WITH GREATER CERTAINTY AND STATISTICAL POWER

- COMPARISON WITH CLINICAL DATABASES CAN PROVIDE IMPORTANT INFORMATION REGARDING COMPETITIVE POSITIONING RELATIVE TO EXISTING THERAPIES

FIG. 10a

FIG. 10b



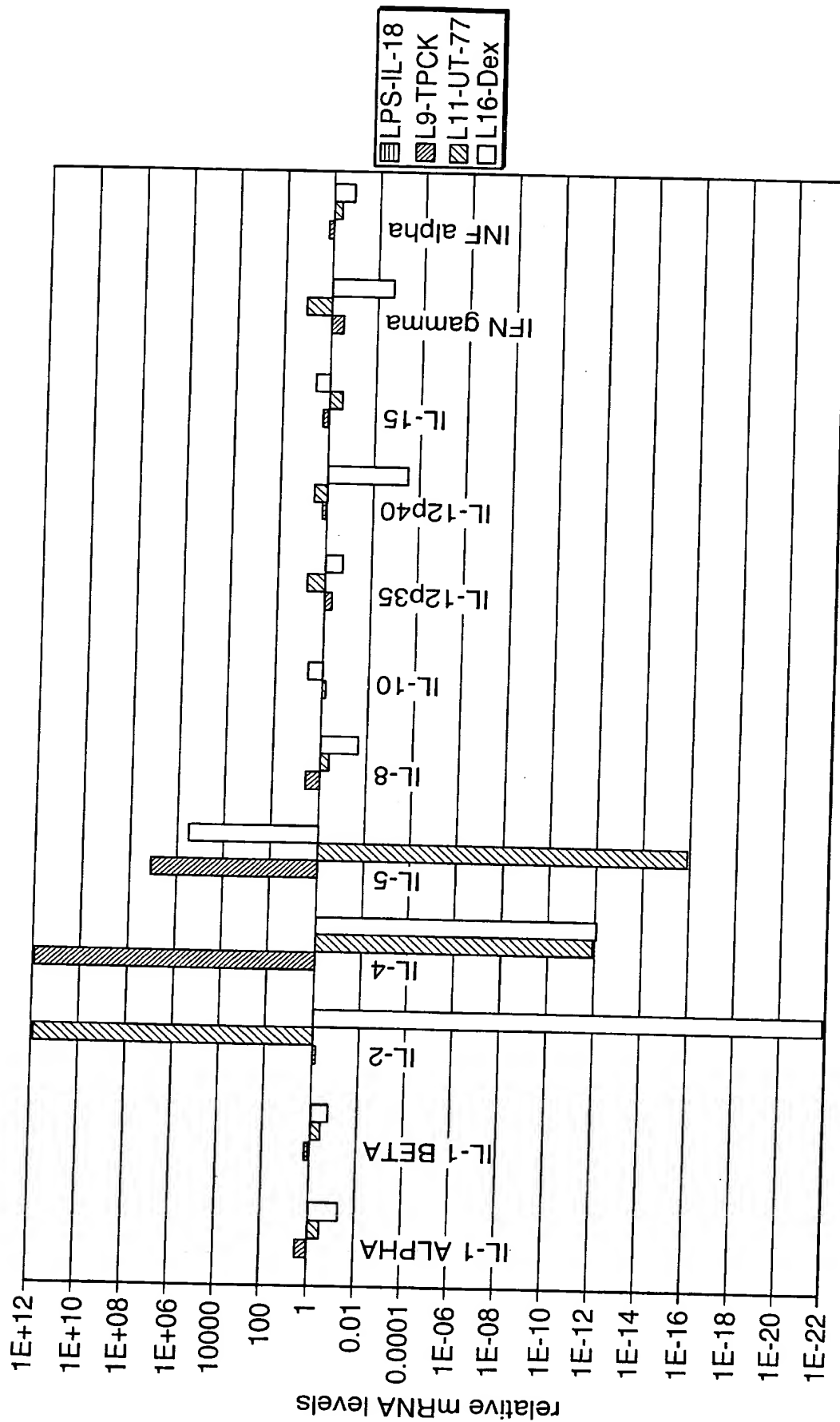


FIG. 11b

# COMPARATIVE DRUG PROFILING SHOWS DIFFERENCES AMONG ANTI- INFLAMMATORY DRUGS WITH DIFFERENT MECHANISM OF ACTION

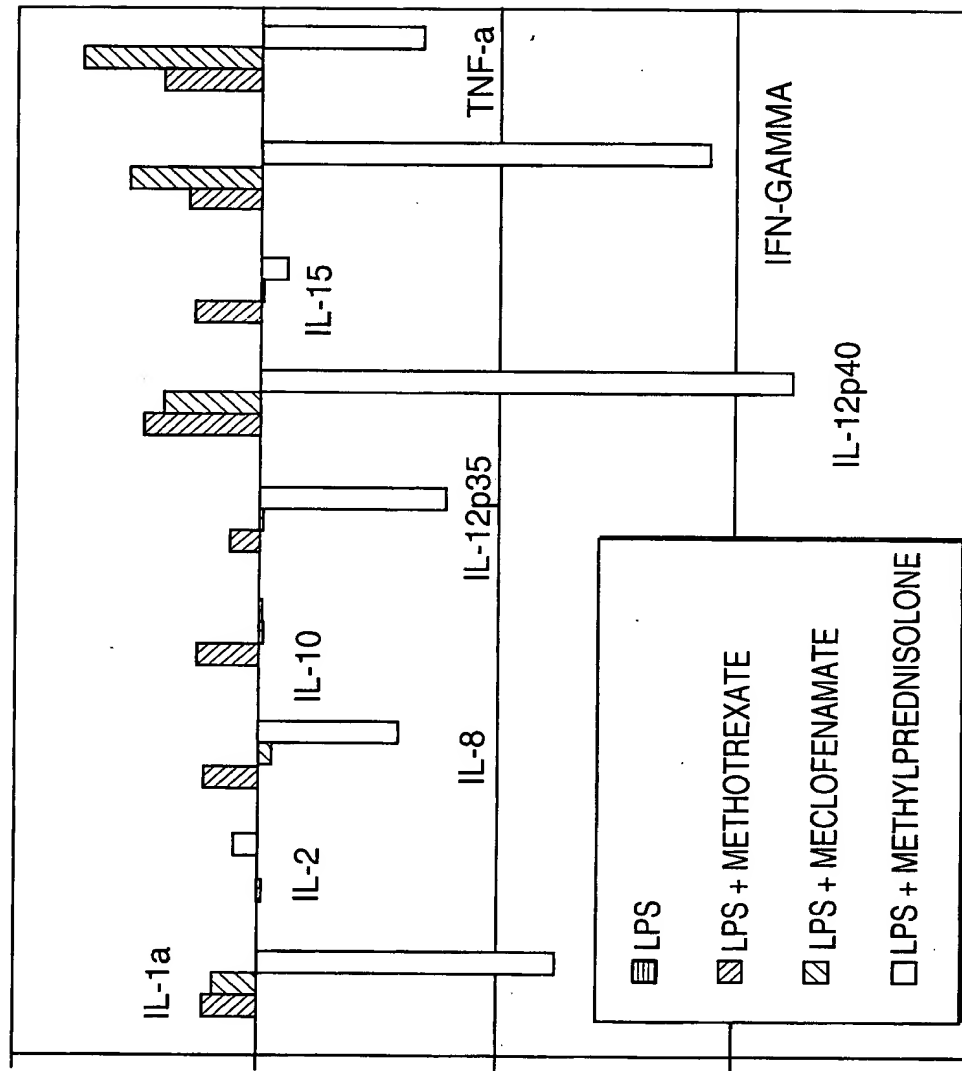


FIG. 12a

# 9911116 LPS, HKS, PHA COMPARATIVE STIMULATION OF WB AT 6 HOURS

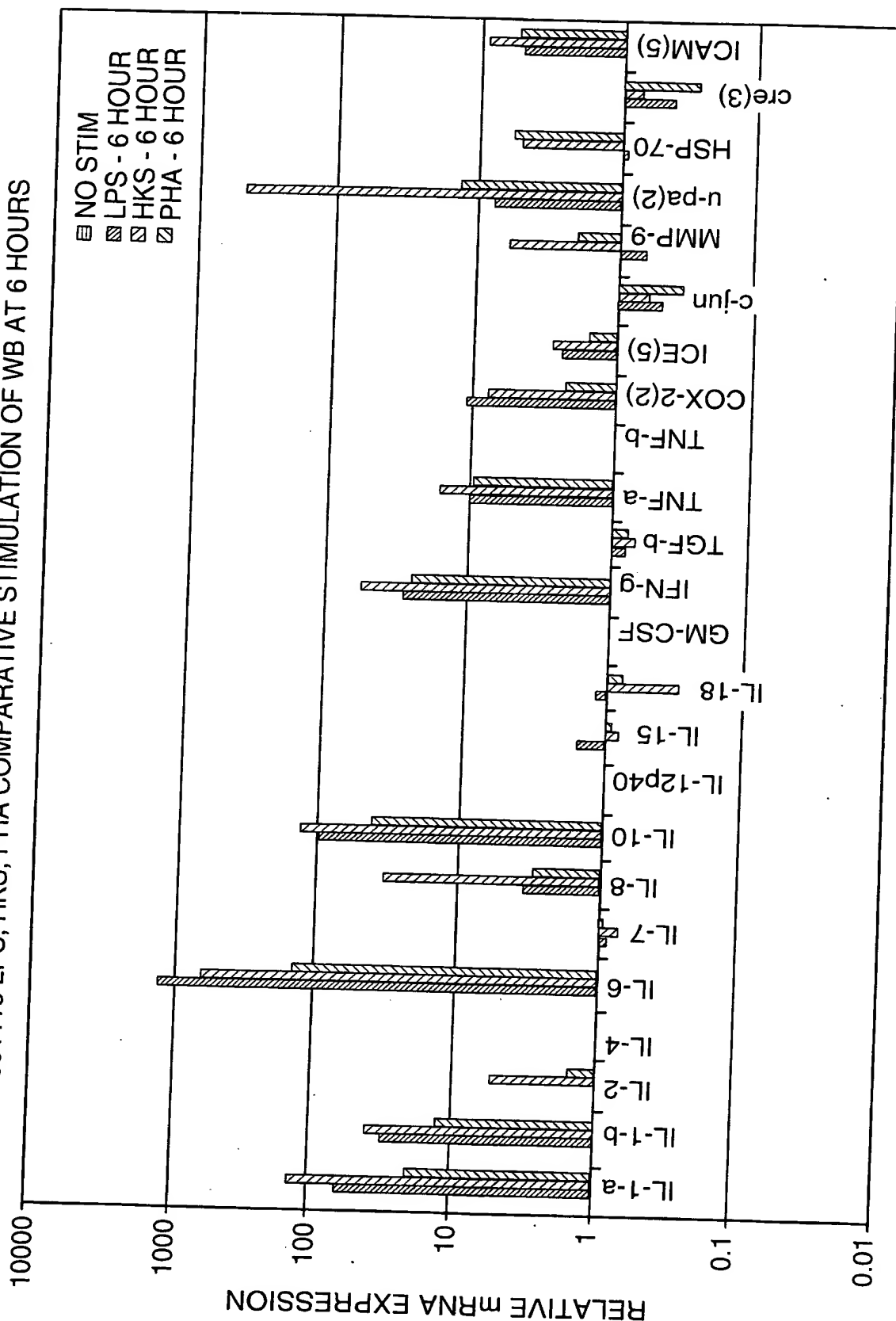


FIG. 13a

991028 LPS, HKS, PHA COMPARATIVE STIMULATION OF WB - 6 HOUR

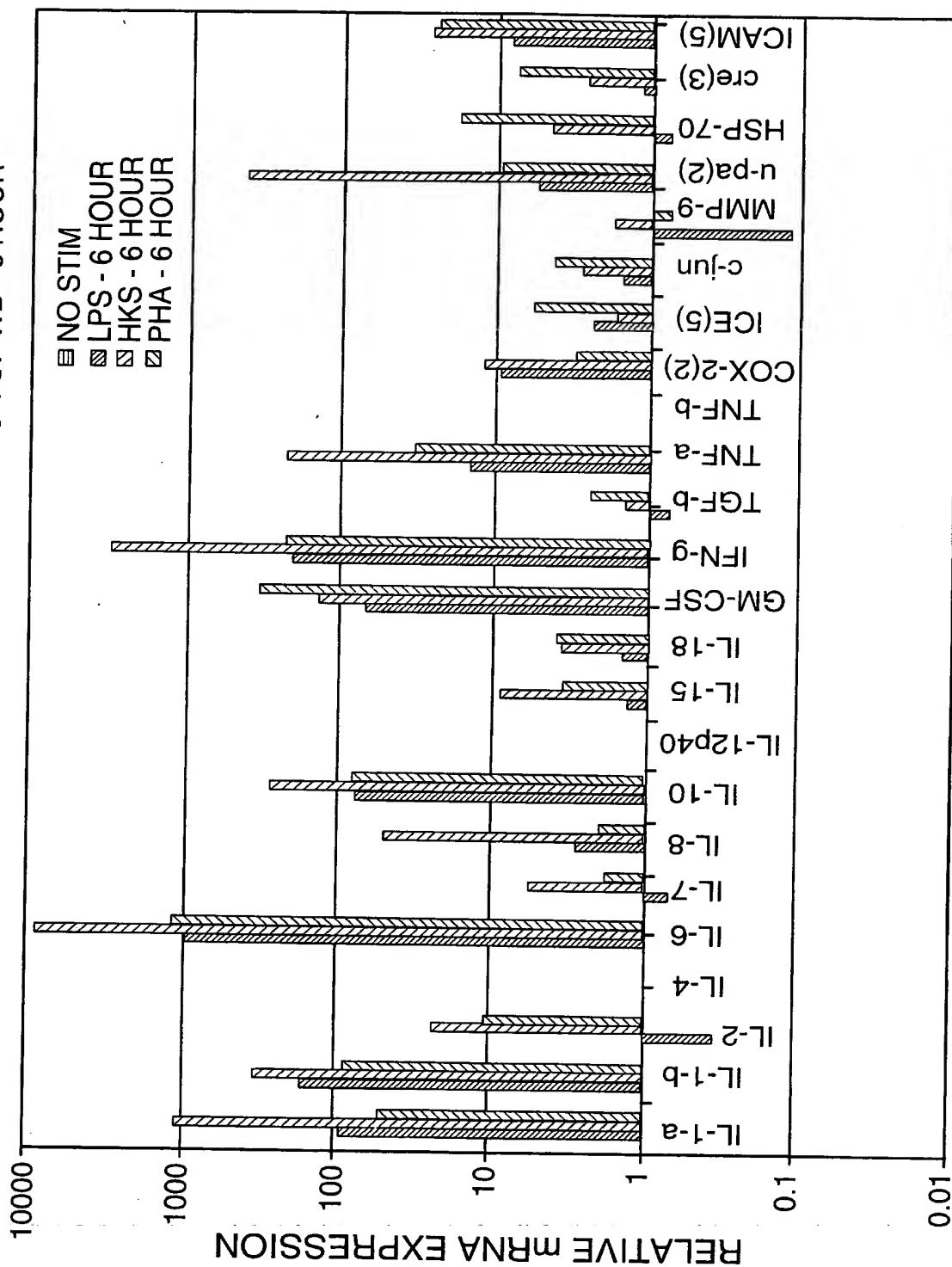


FIG. 13b





INDIVIDUAL COMPARISON OF DONOR SAMPLE WITH NO STIMULATION  
6 HOUR - 991028 VS. 991116 DONOR: TK

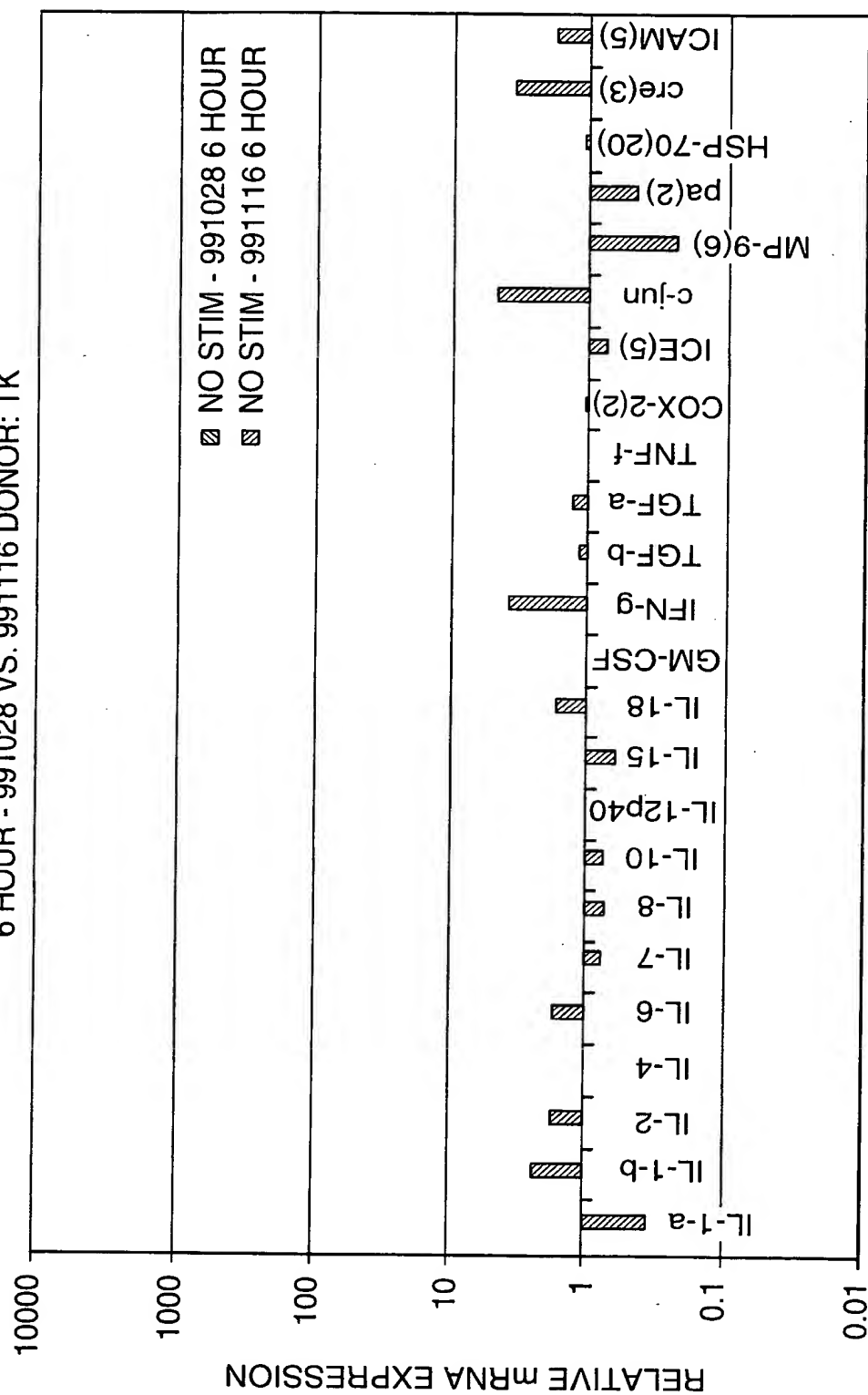


FIG. 13d

FIG. 13d

STIMULANT EFFECT ON METHYL PREDNISOLONE GENE EXPRESSION IN WHOLE BLOOD - 6 HOUR

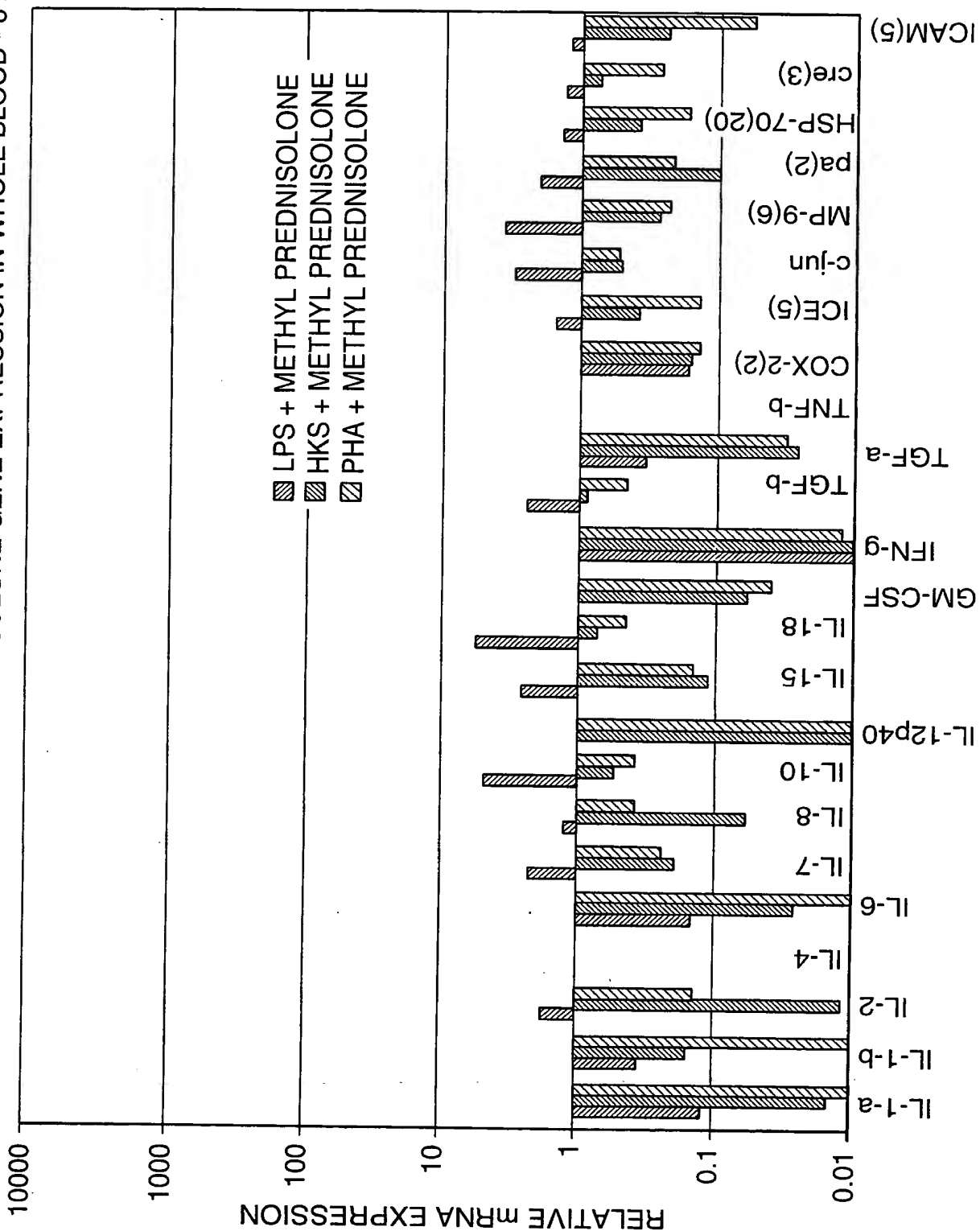


FIG. 14

COMPARISON OF IN VITRO AND IN VIVO GENE EXPRESSION IN RESPONSE TO  
CORTICOSTEROID TREATMENT

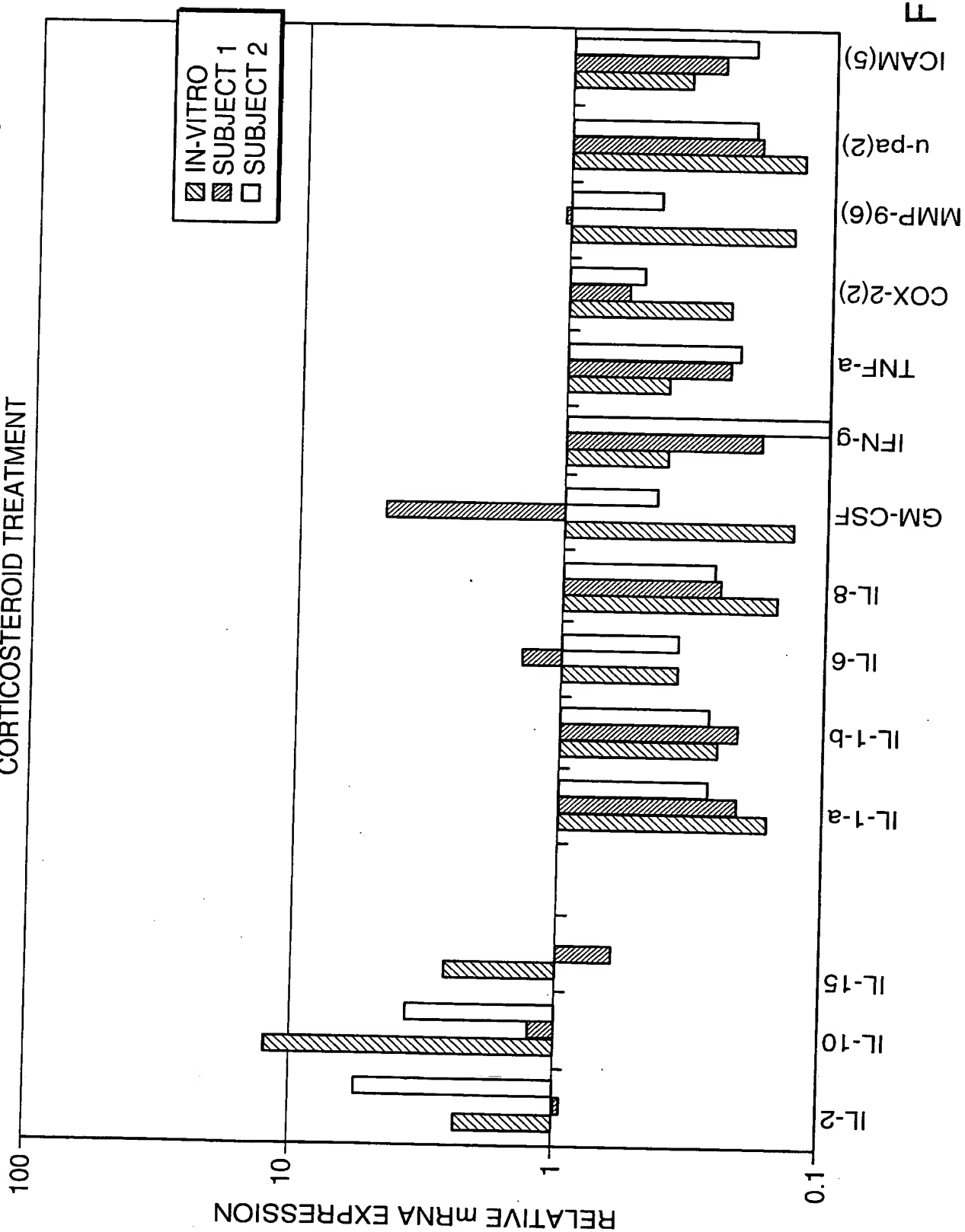


FIG. 15

**THE** **NEW** **YORK** **PUBLIC** **LIBRARY**

**ASTOR LENOX TILDEN FOUNDATION**

**100 N. Y. ST.**

**NEW YORK**

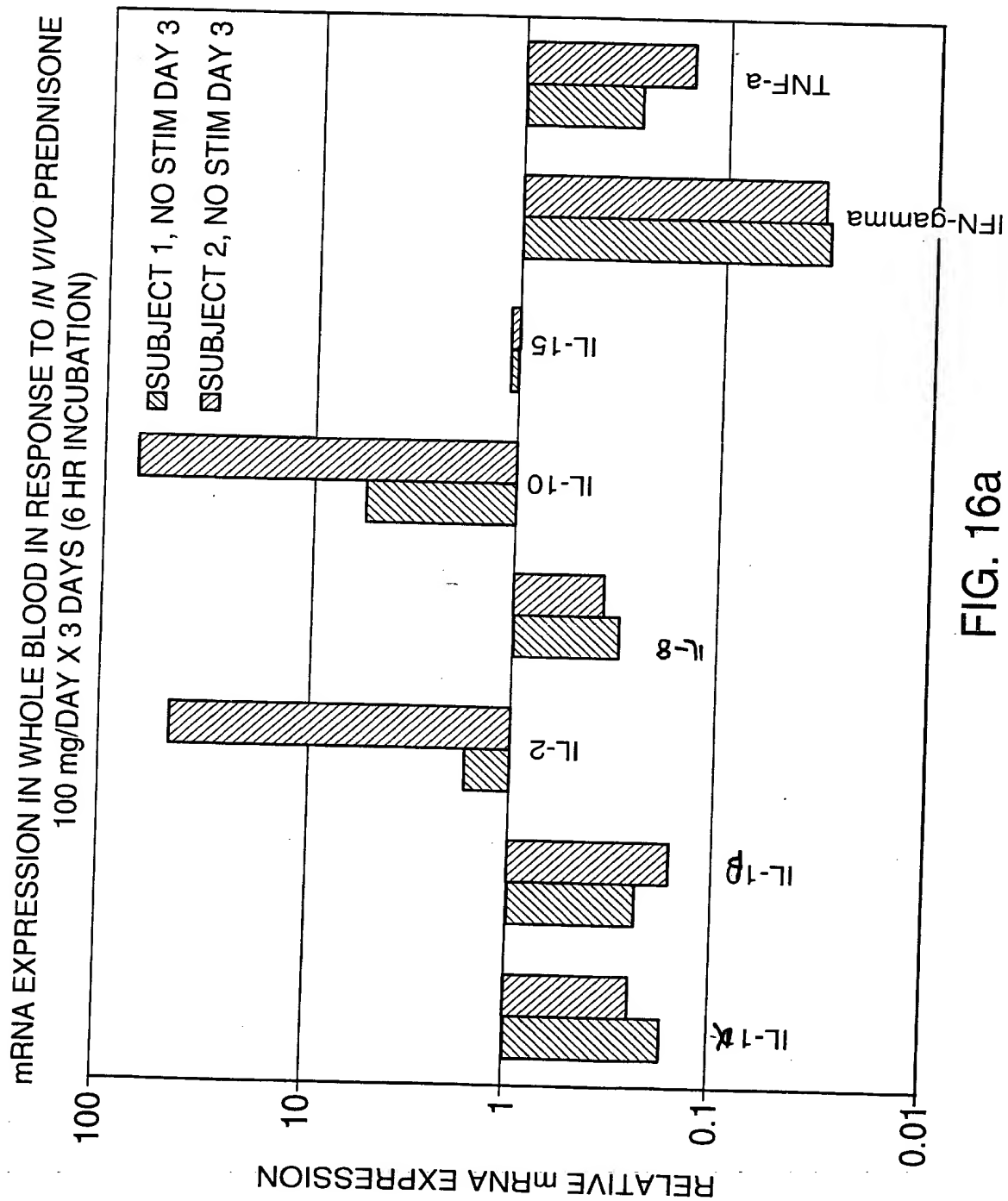


FIG. 16a

mRNA EXPRESSION IN WHOLE BLOOD IN RESPONSE TO *IN VIVO* PREDNISONE  
100 mg/DAY X 3 DAYS (1.5 HR INCUBATION)

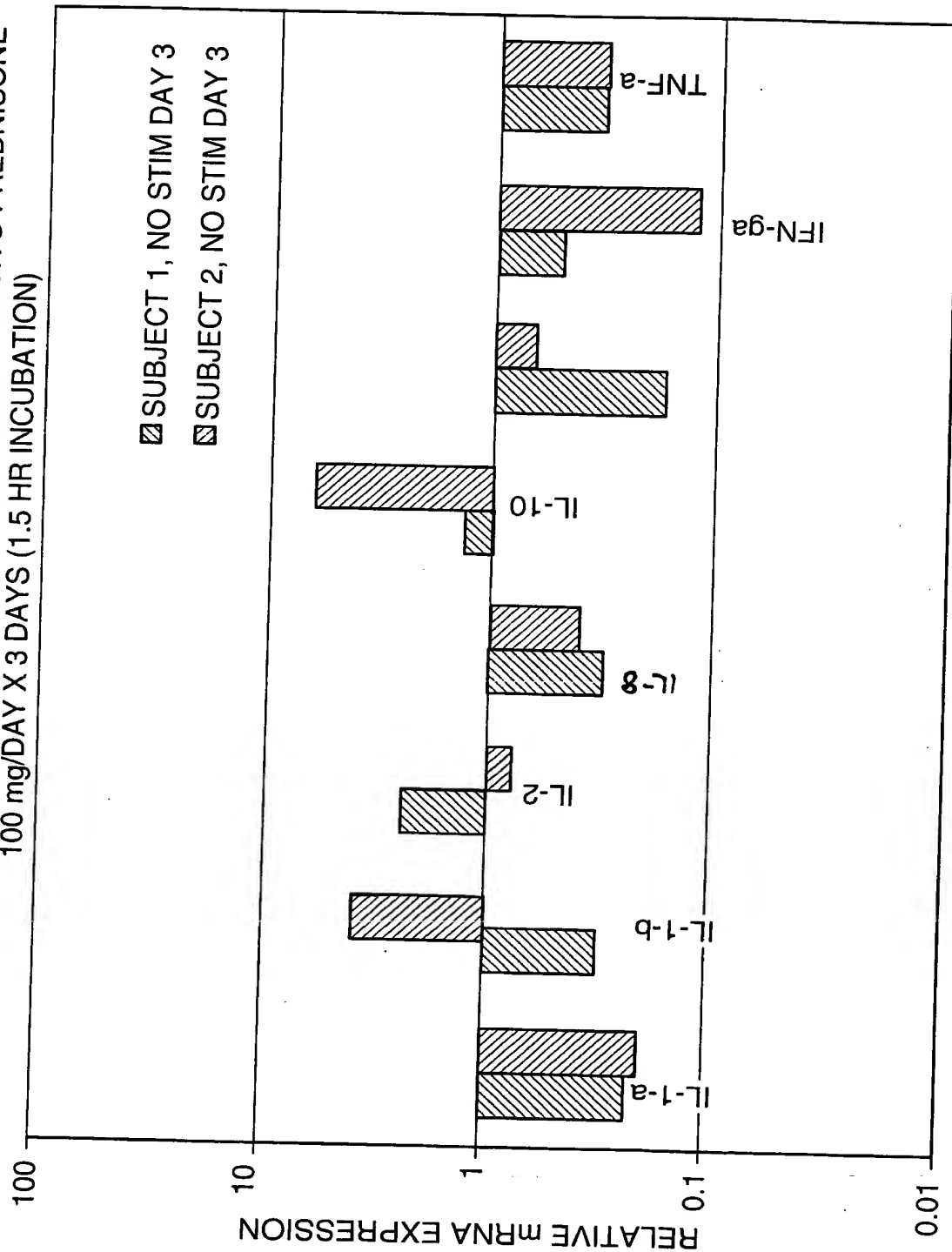


FIG. 16b

INDIVIDUAL COMPARISON - 991028 VS. 991116  
DONOR: TK

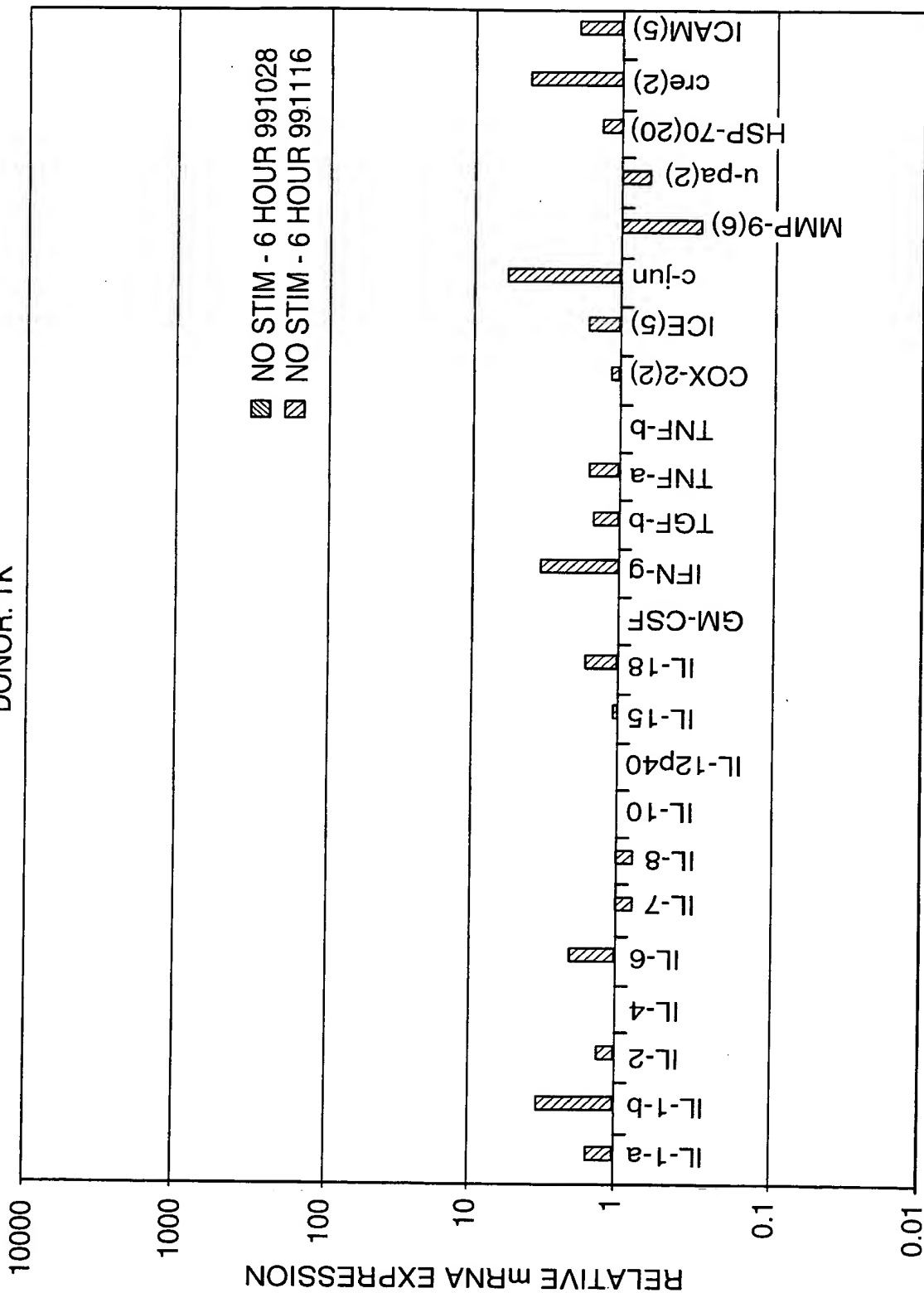


FIG. 17



PB001 STUDY 2, STAGE 3  
 EFFECTS OF DRUG ON WHOLE BLOOD  
 DONOR 2

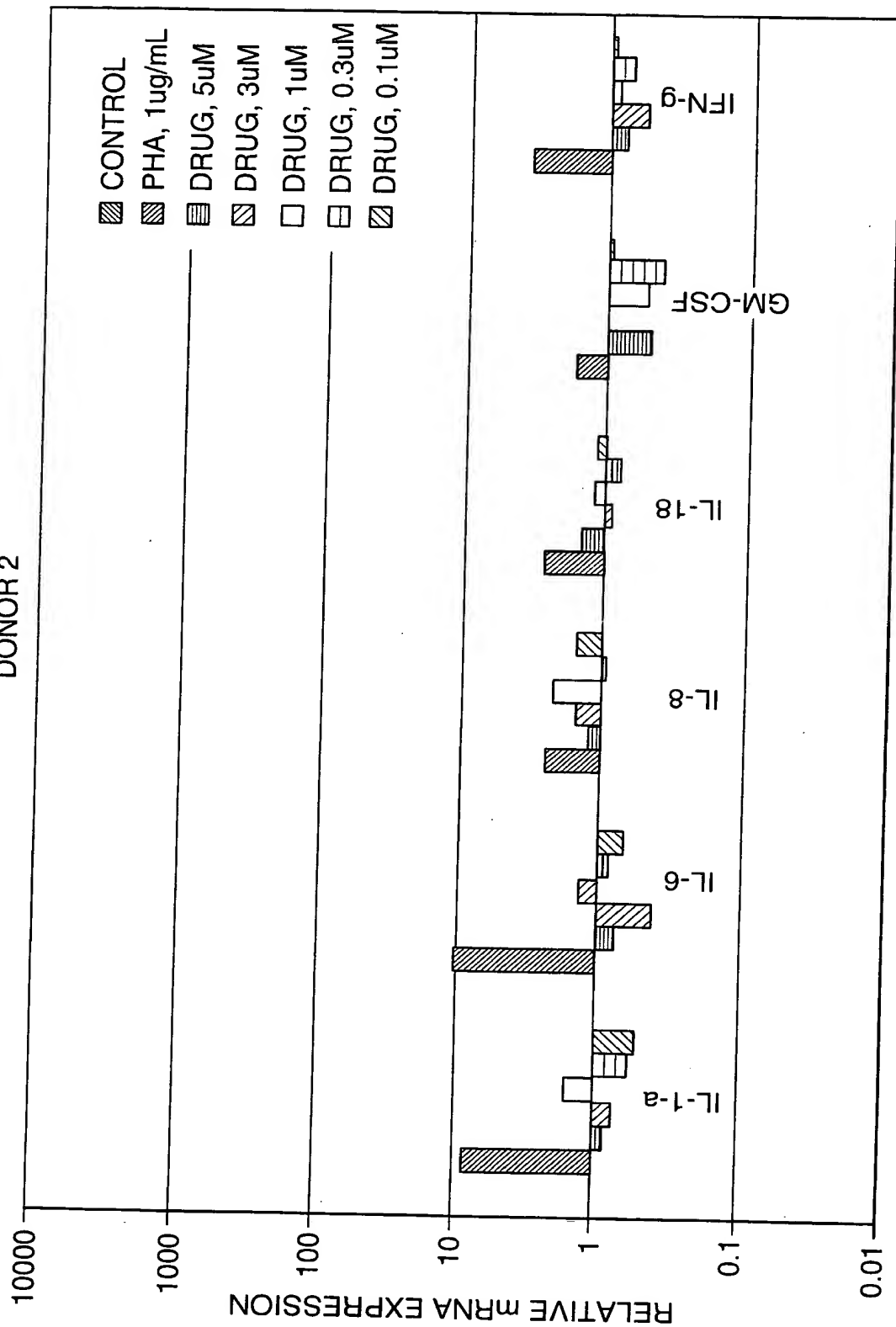


FIG. 18b



PB001 STUDY 2, STAGE 3  
EFFECTS OF DRUG ON WHOLE BLOOD  
DONOR 3

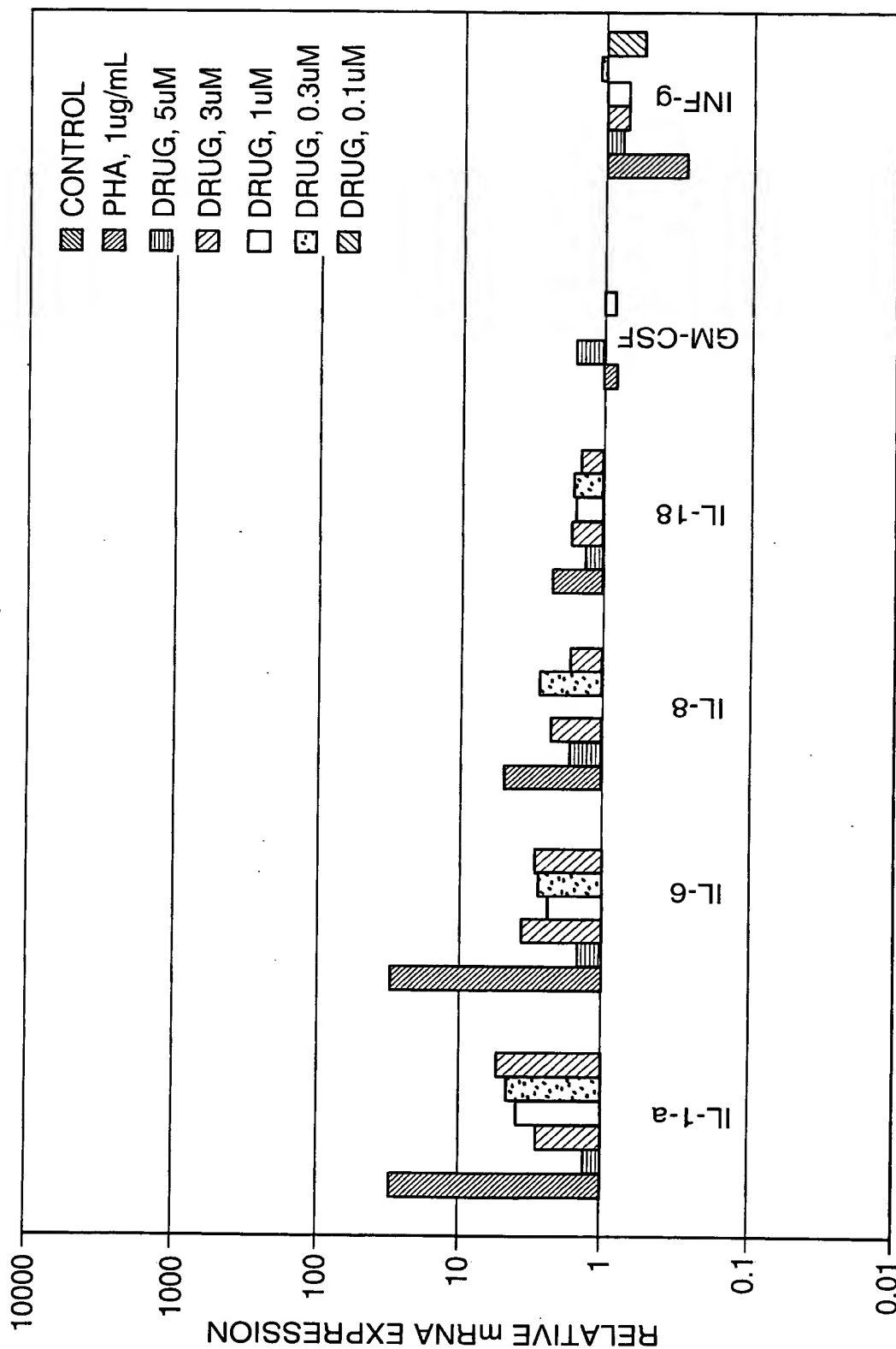


FIG. 18c

PB001 STUDY 2, STAGE 3  
 EFFECTS OF DRUG ON WHOLE BLOOD  
 DONOR 4

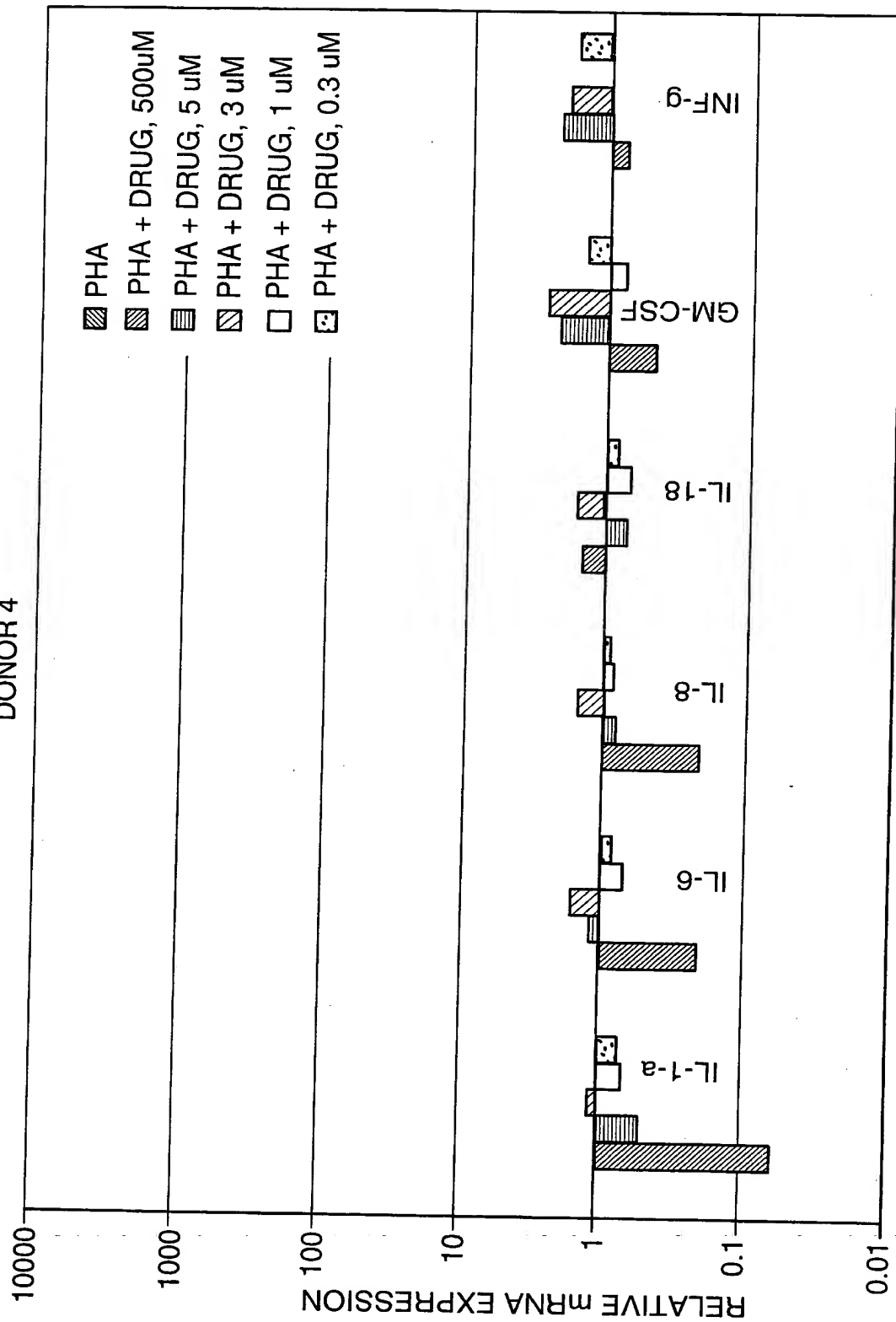


FIG. 18d

PB001 STUDY 2, STAGE 3  
EFFECTS OF DRUG ON WHOLE BLOOD  
DONOR 5

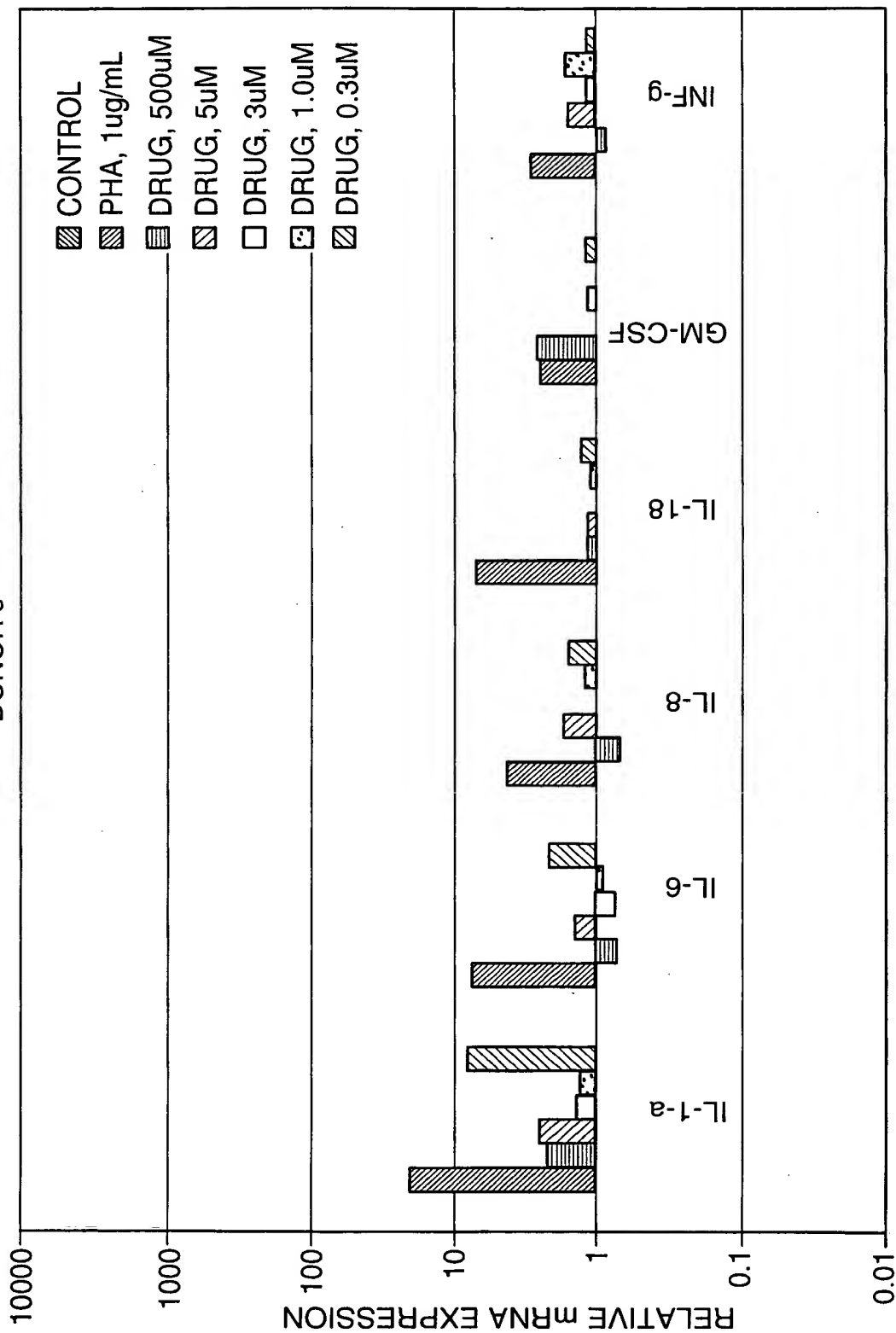


FIG. 18e

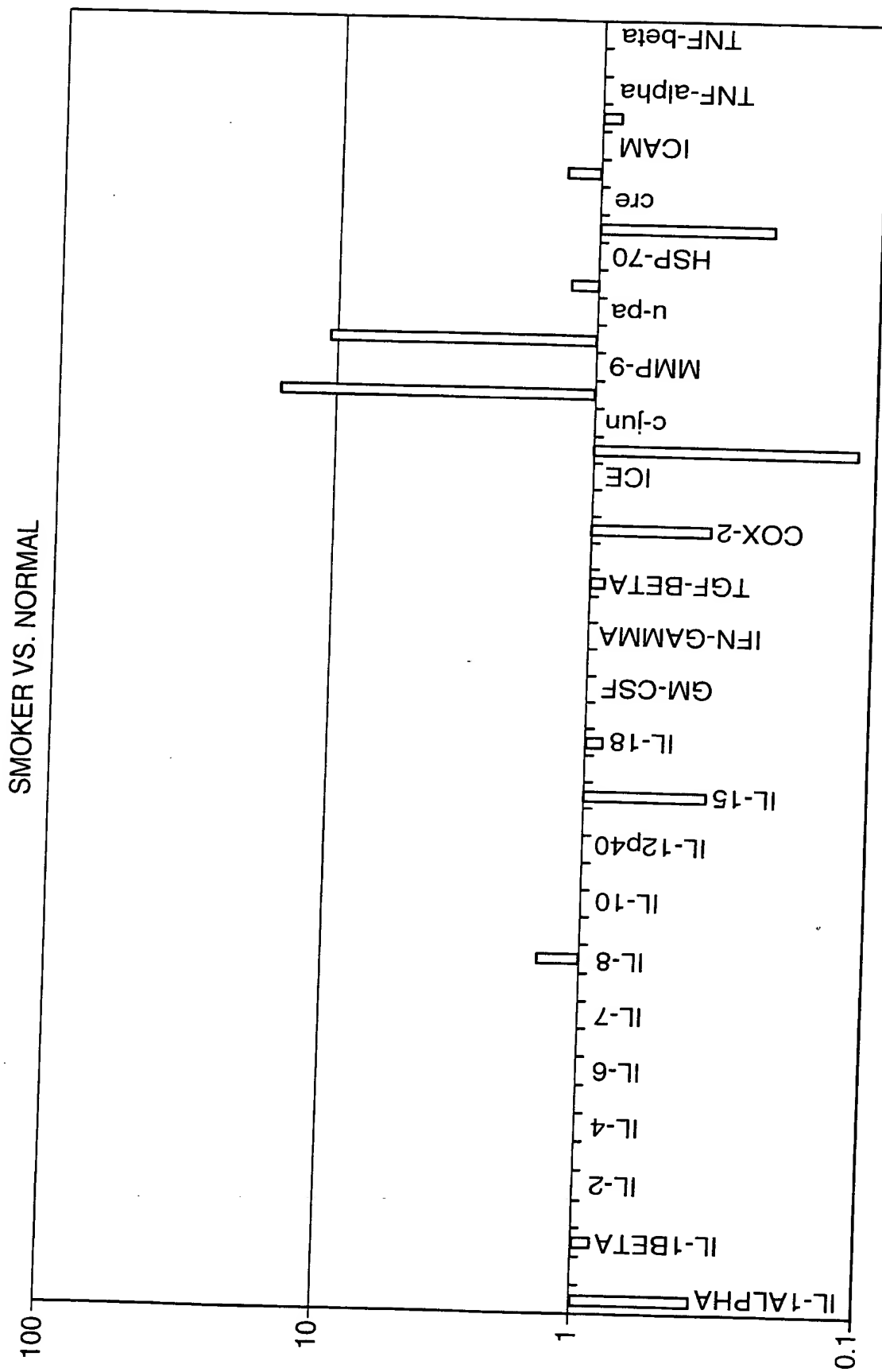


FIG. 19a

NAC PATIENT VS. NORMAL

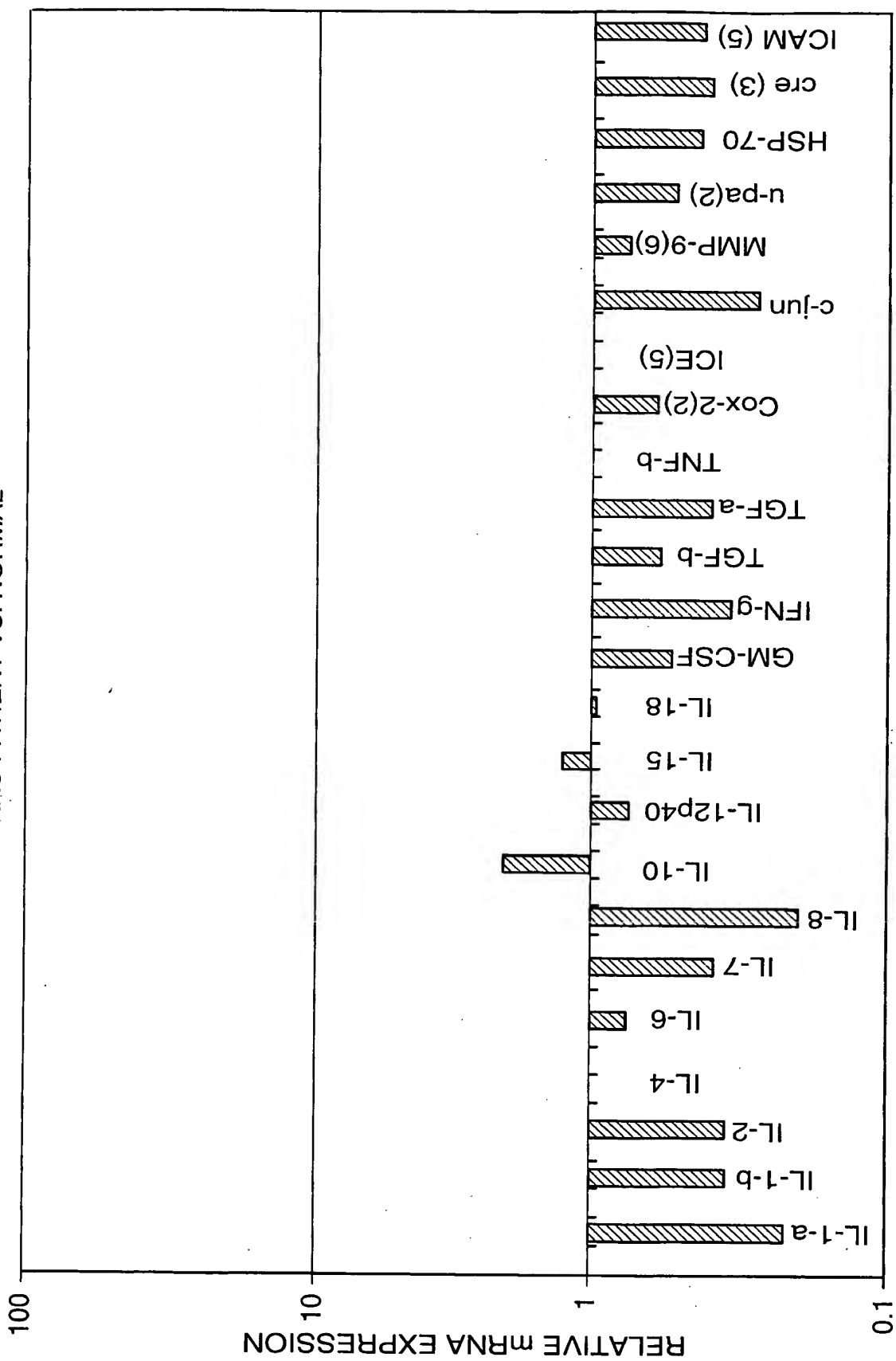


FIG. 19b

EXPRESSION OF GST-P GENE IN INDIVIDUAL RATS FOLLOWING A TOXIC DOSE OF ACETAMINOPHEN

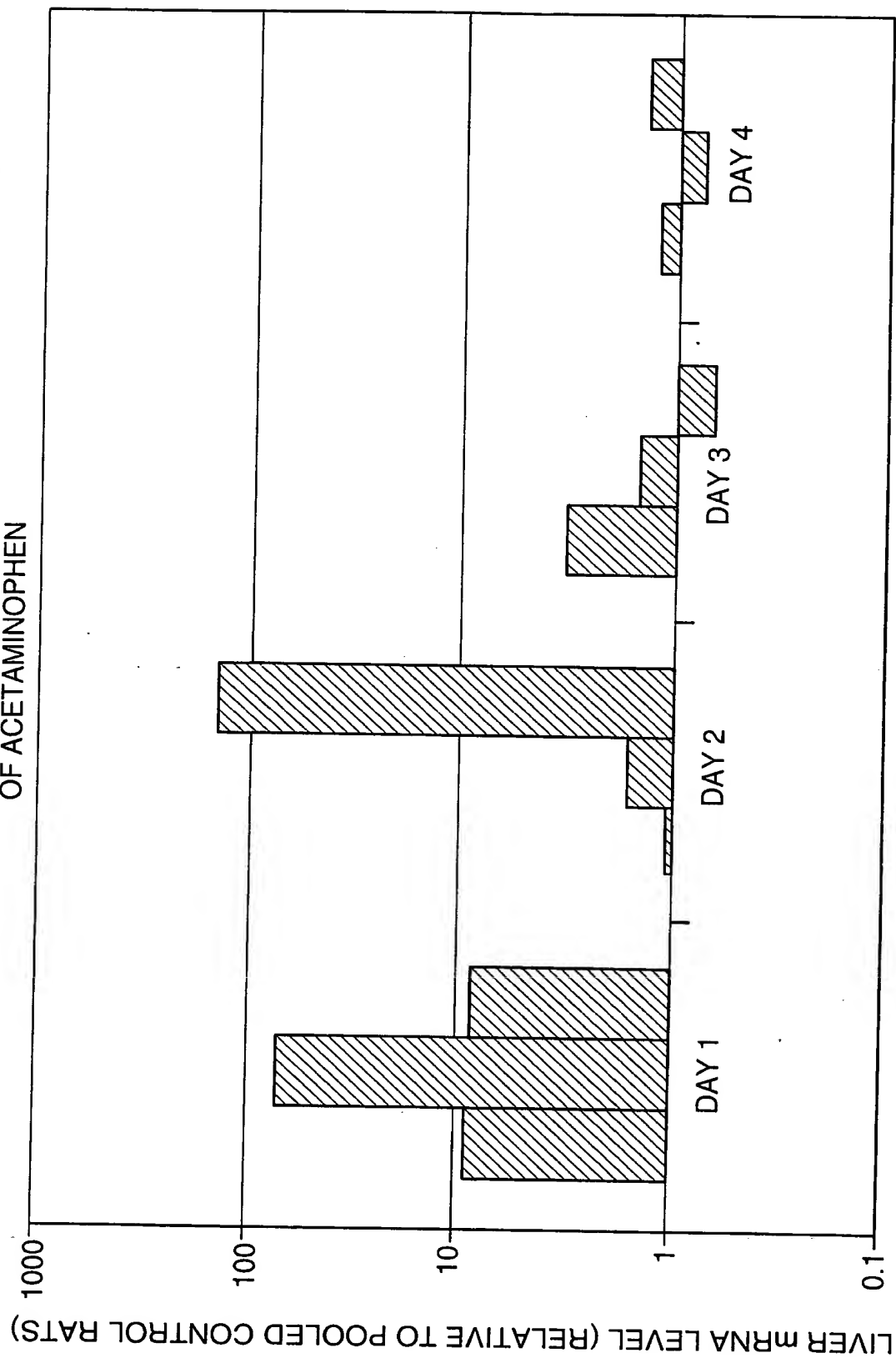


FIG. 20

COMPARATIVE HERBAL PROFILING SHOWS DIFFERENCES AMONG ANTI-INFLAMMATORY HERBS SUCH AS ECHINACEA, ARNICA AND SIBERIAN GINSENG

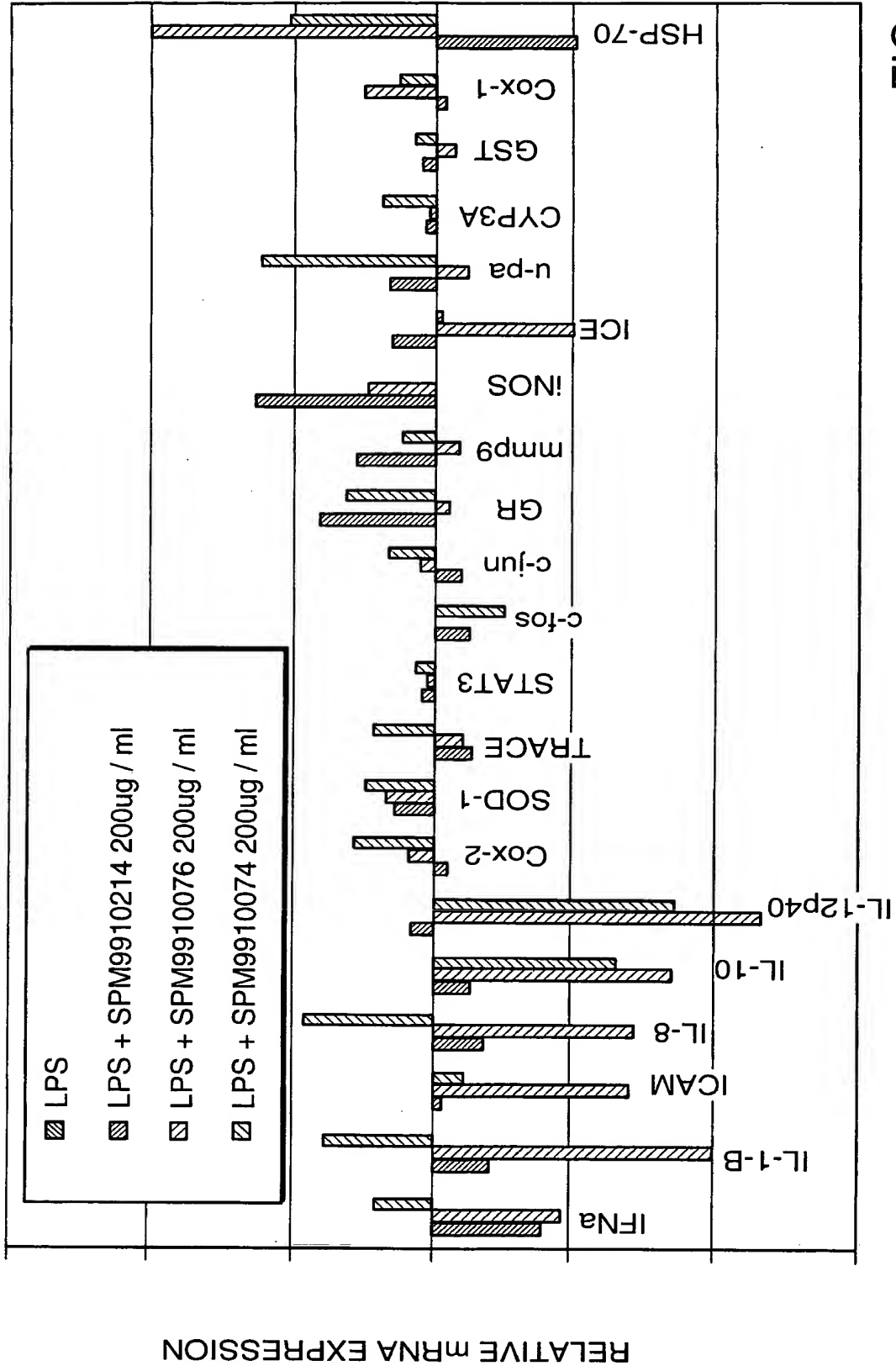


FIG. 21

991203 WHOLE BLOOD 6HR

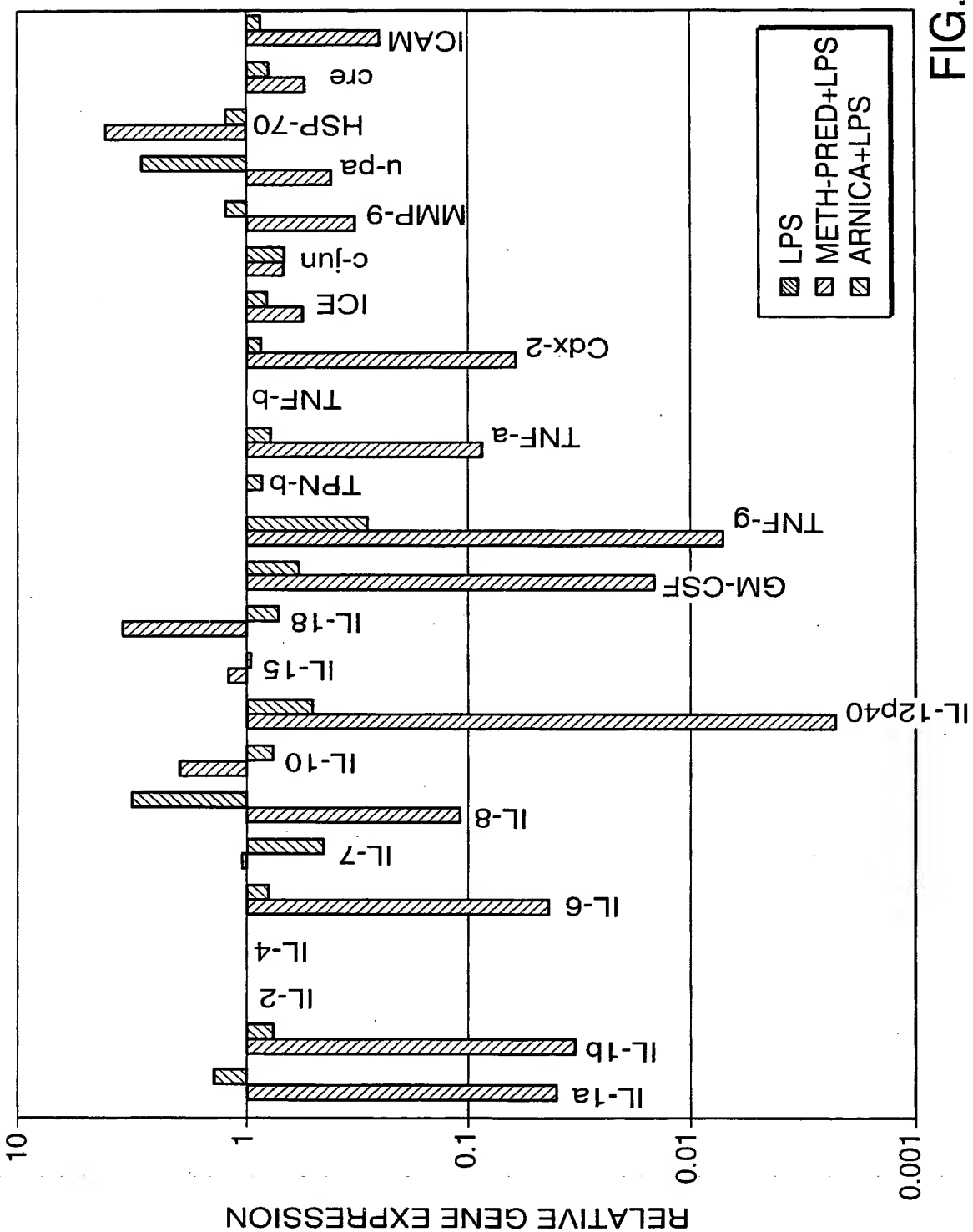


FIG. 22



PRECISION PROFILES CAN CORRELATE WITH A DOSE RESPONSE FOR A GIVEN HERBAL

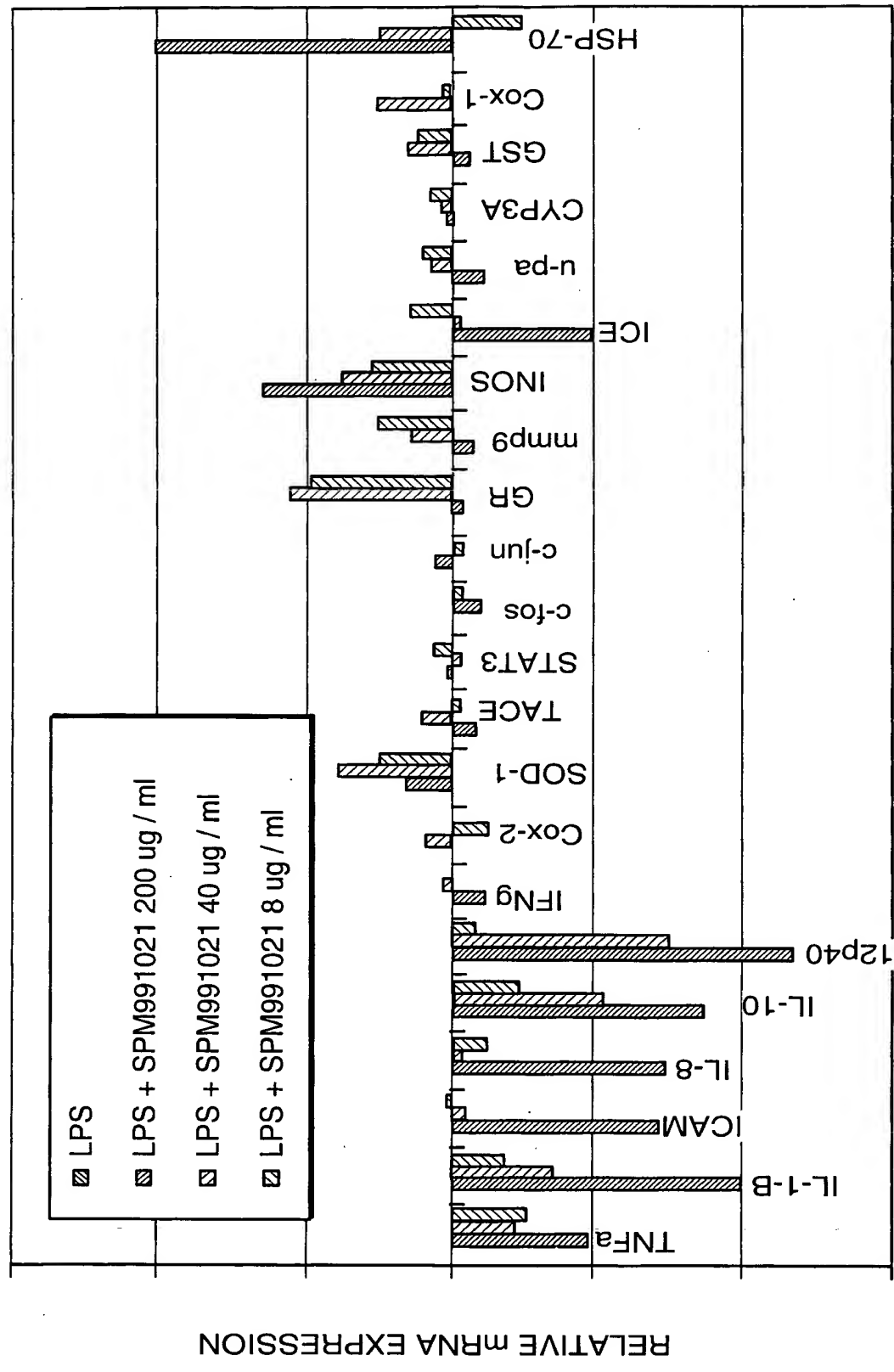


FIG. 23

PRECISION PROFILES REVEAL CONTAMINATION WITH ENDOTOXIN  
AMONG DIFFERENT COMMERCIAL BRANDS AS REVEALED IN SPM010  
AND SPM016

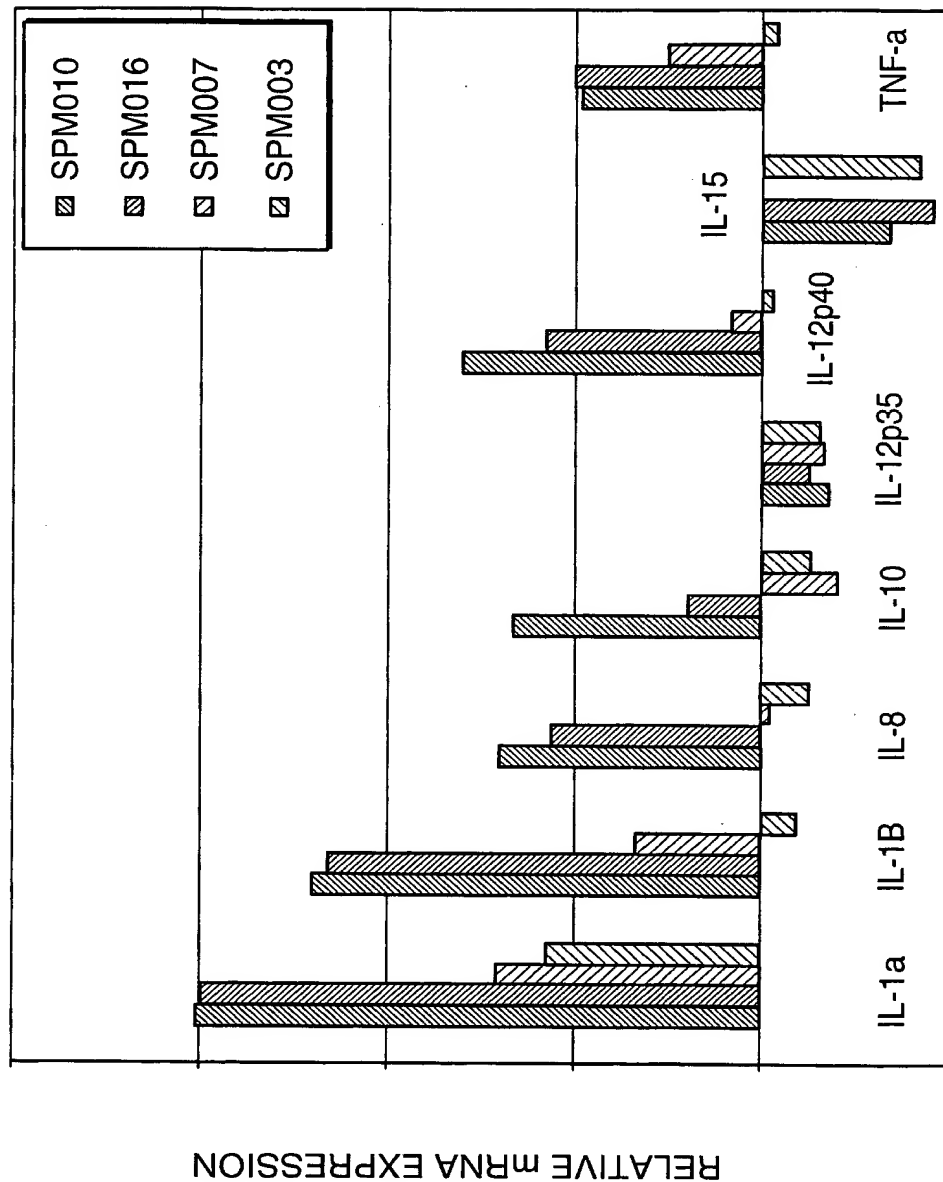


FIG. 24

# HIGH DOSE COMPARISON OF UNSTIMULATED THP-1 CELL TREATMENT WITH THREE HERBAL PREPARATIONS SHOWS SIGNIFICANT VARIATION IN EFFICACY

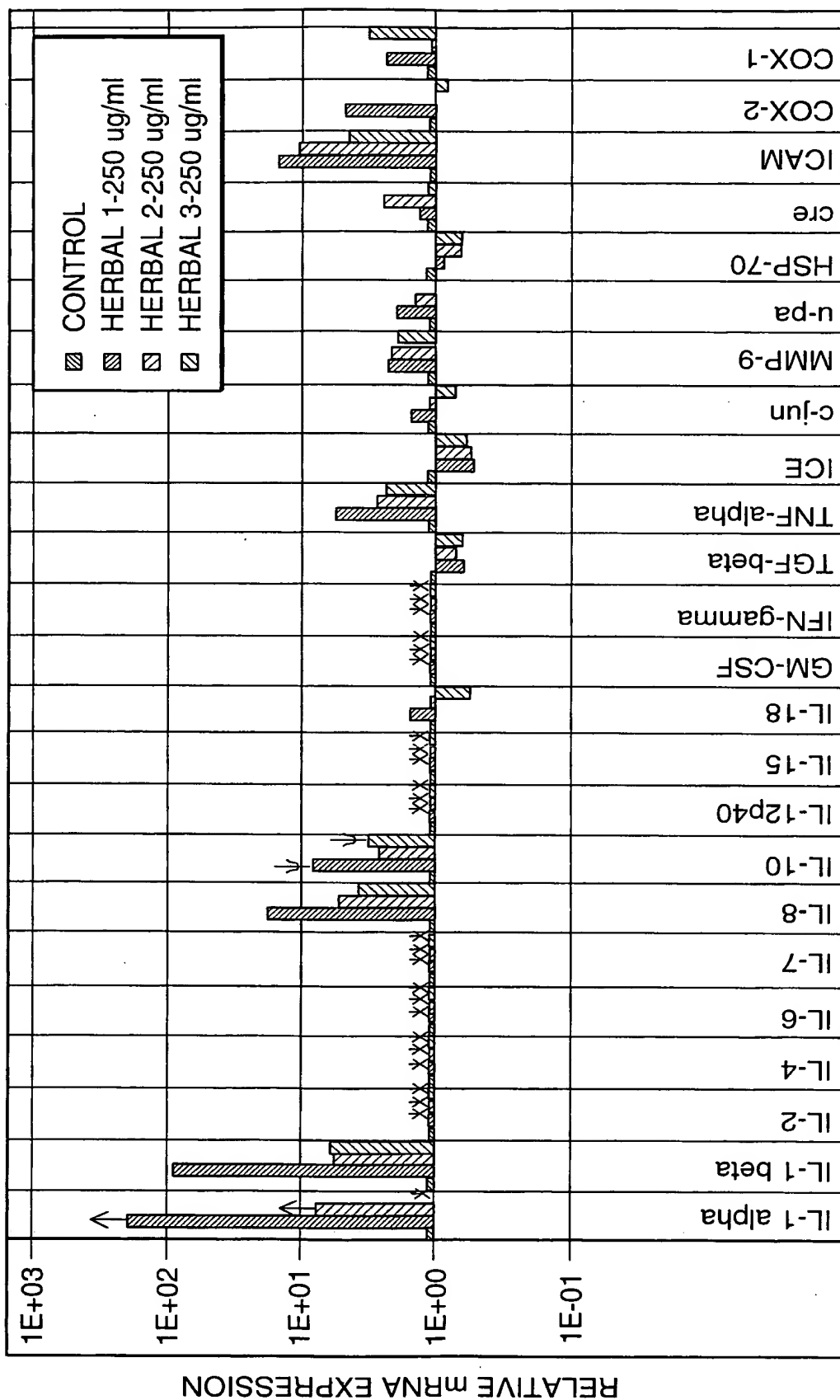


FIG. 25a

TREATMENT OF UNSTIMULATED THP-1 CELLS WITH A SINGLE  
HERBAL SHOWS A NICE DOSE RESPONSE AMONG A SUBSET OF  
GENES

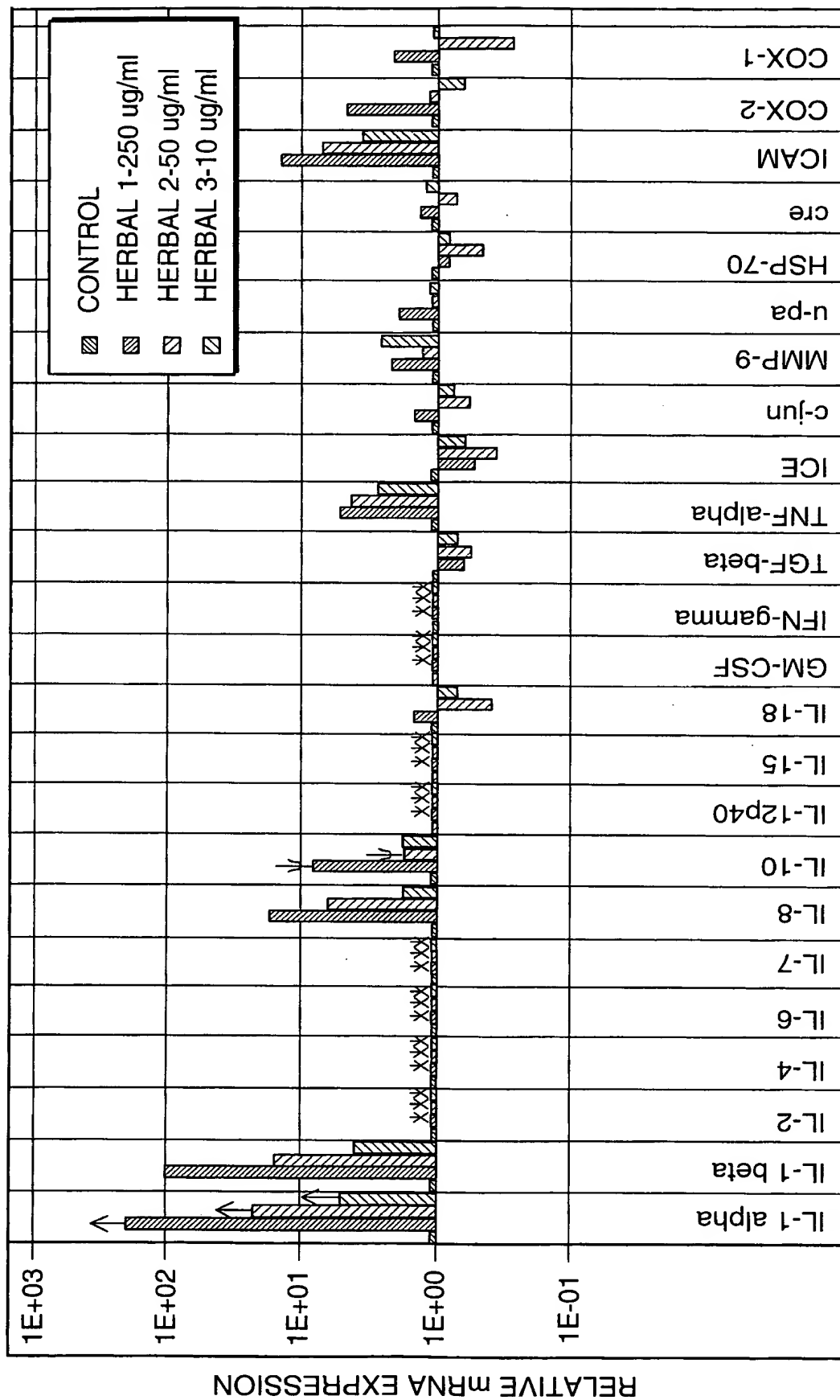


FIG. 25b

PRECISION PROFILES ALLOW FOR COMPARISON OF  
COMMERCIAL ECHINACEAS (E1-E4)

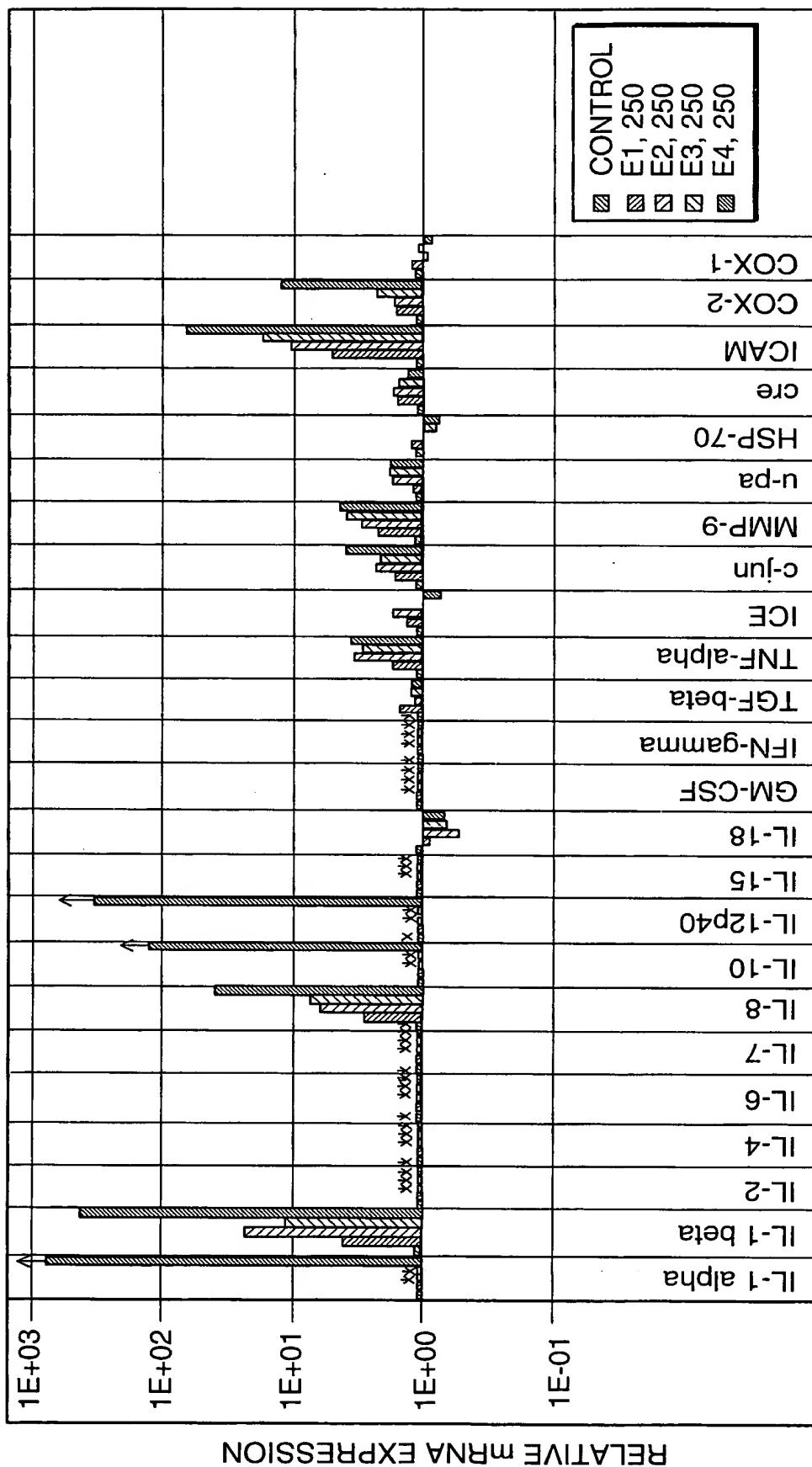


FIG. 25c

Figure 26. Inflammation Precision Panel Subset Demonstrates Steroid Response in 3 Day Study

Figure 26(a)

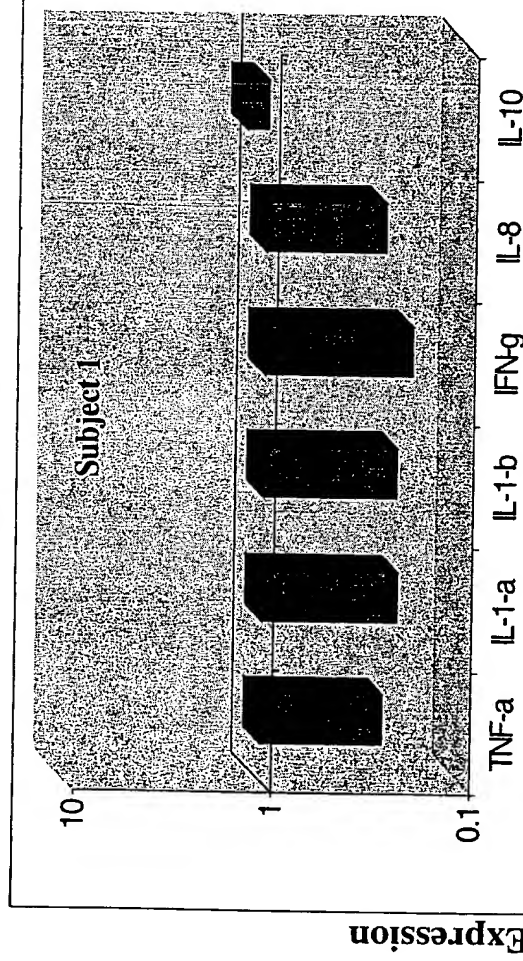


Figure 26(b)

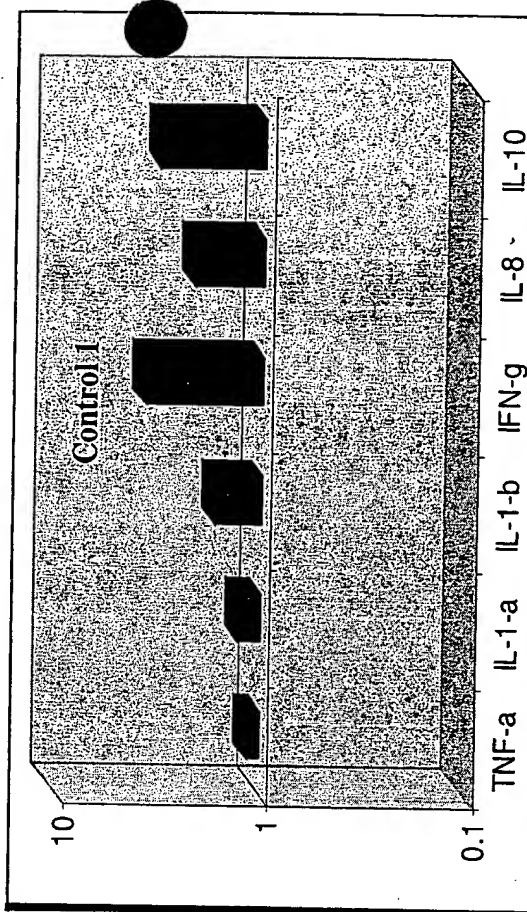


Figure 26(c)

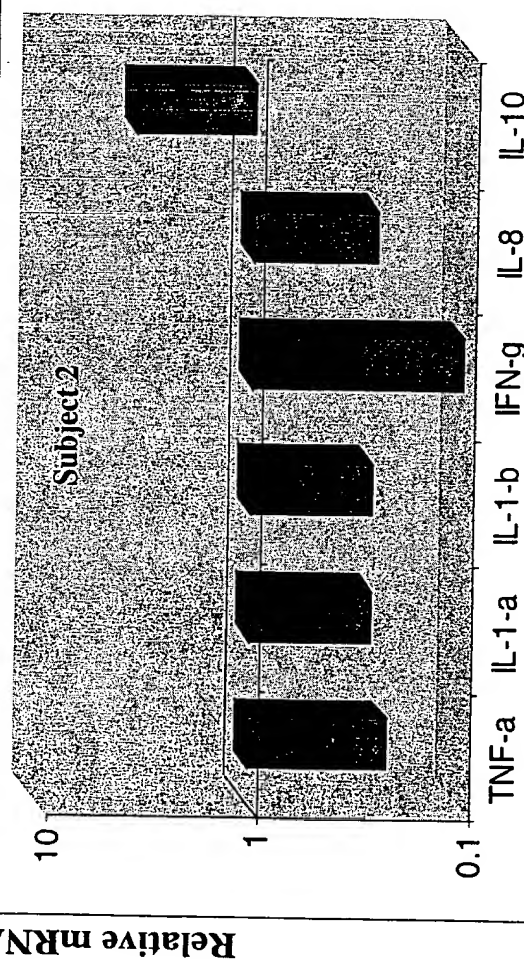


Figure 26(d)

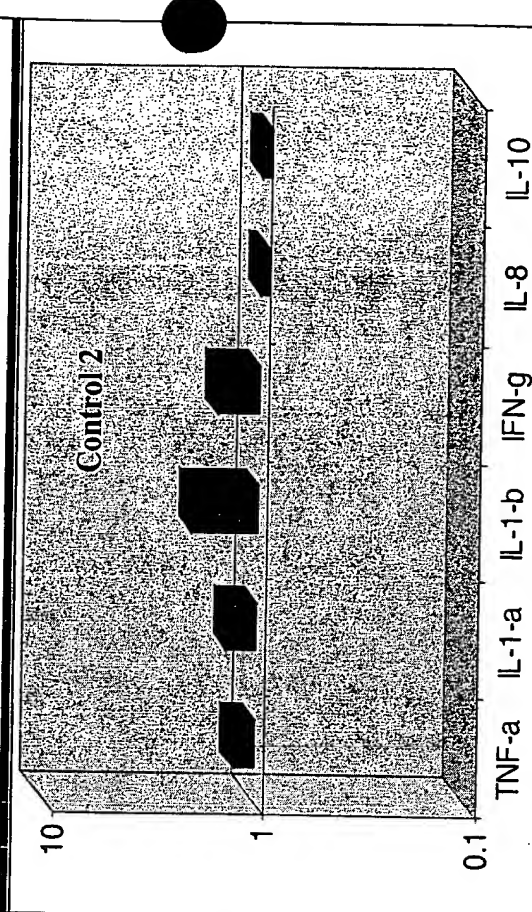


Figure 27. Comparison of Methylprednisone and High-Dose Ibuprofen in Patients Using Inflammation Precision Panel Subset

Figure 27(a)

### Methylprednisone

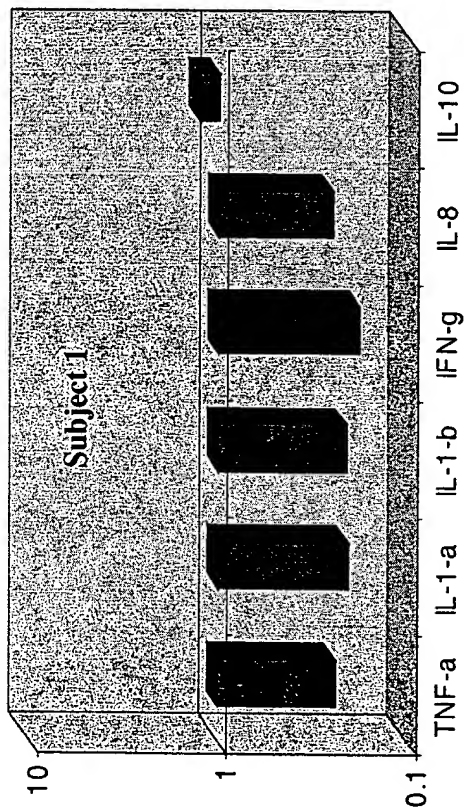


Figure 27(b)

### Ibuprofen

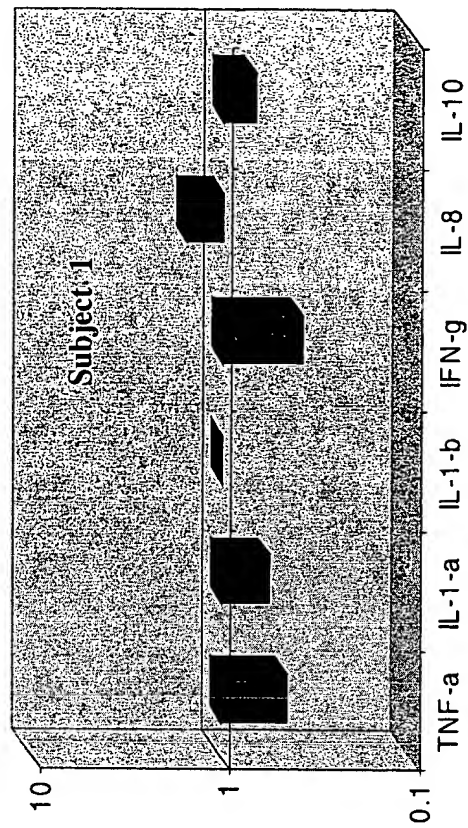


Figure 27(c)

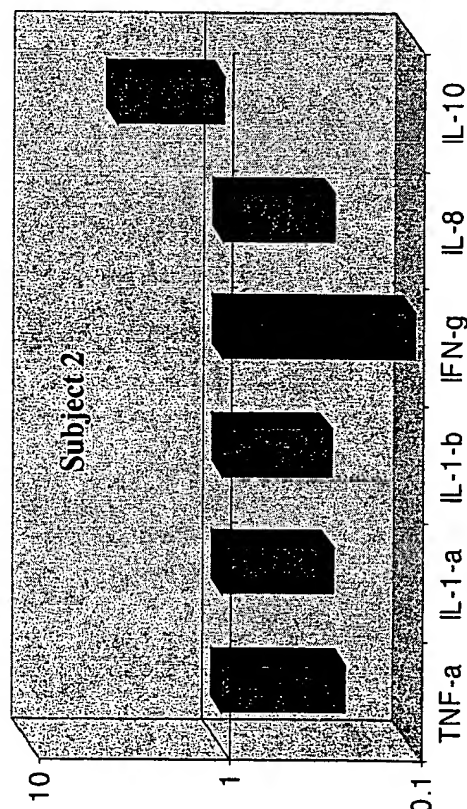


Figure 27(d)

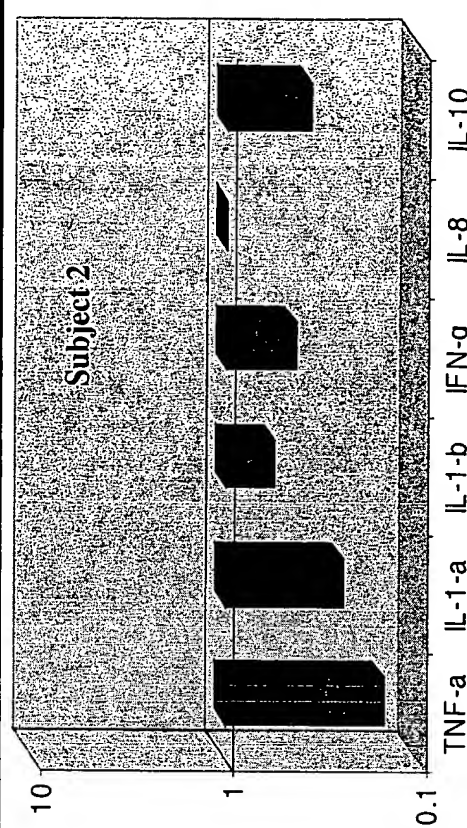




Figure 28. Inflammation Precision Panel Subset Identifies COPD Patients

Figure 28(a)

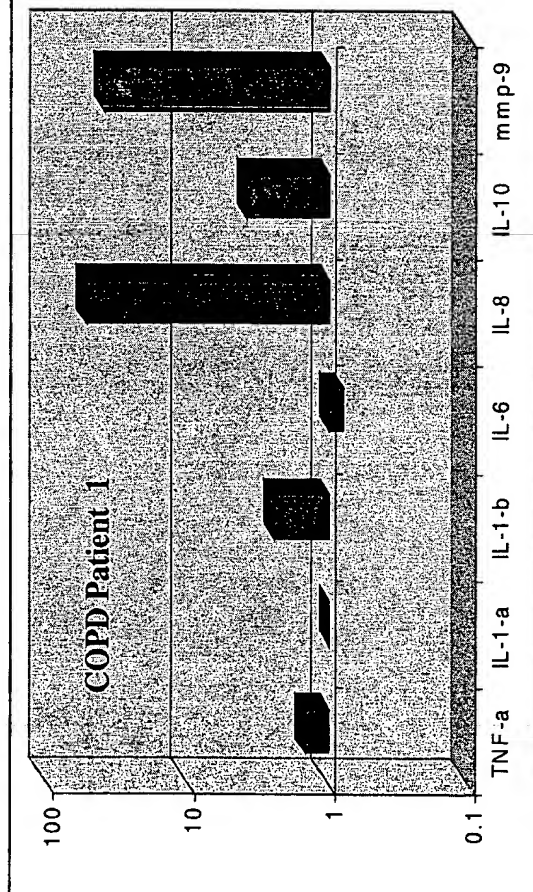


Figure 28(b)

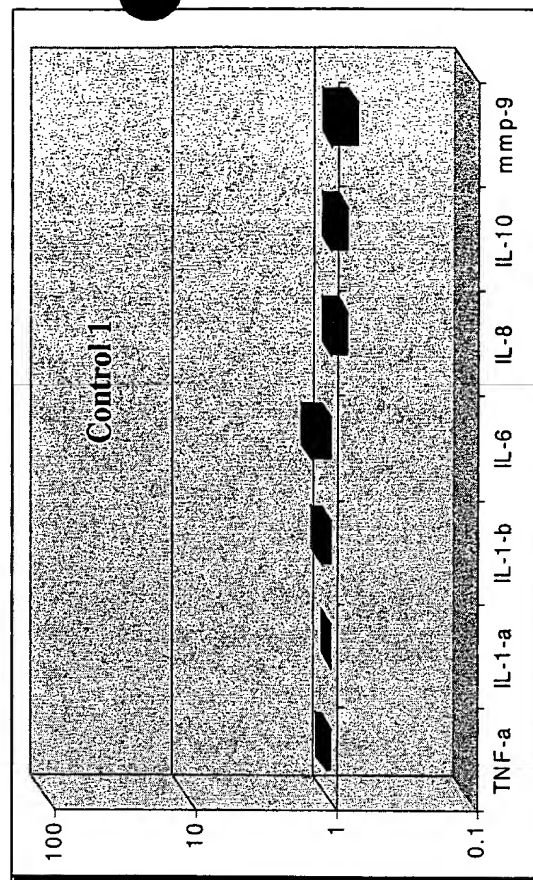


Figure 28(c)

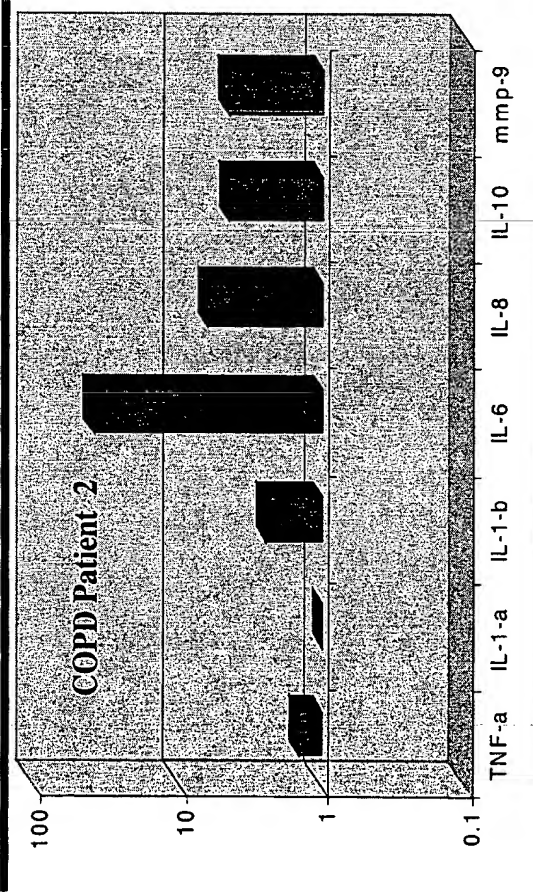
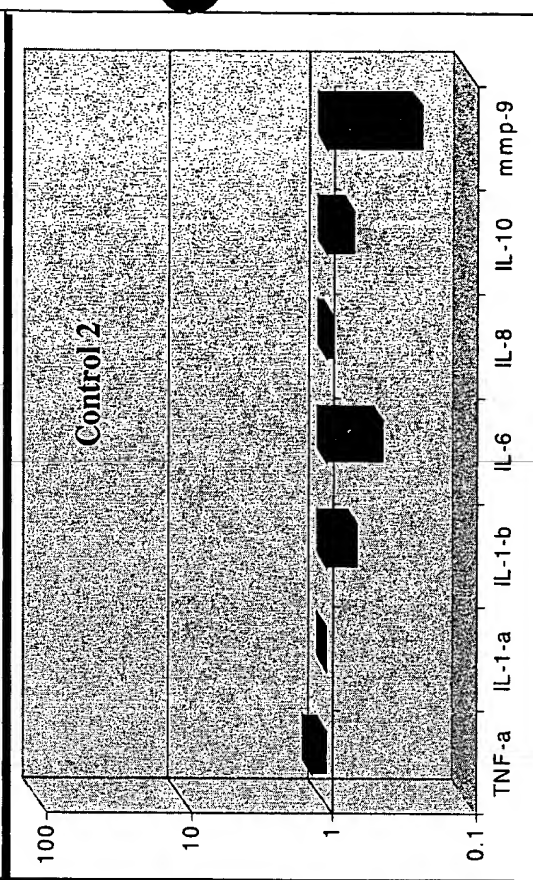


Figure 28(d)





Relative mRNA Expression

Legend:   
 □ in vitro treatment of whole blood   
 ■ in vivo

Gene	in vitro treatment of whole blood	in vivo
ICAM	~1.0	~1.5
HSP-70	~1.5	~2.5
MMP-9	~10.0	~15.0
c-jun	~2.0	~3.0
COX2	~1.0	~1.2
TNF $\alpha$	~1.0	~1.5
IFN $\gamma$	~0.01	~0.01
IL-10	~1.5	~2.0
IL-8	~1.0	~1.2
IL-1 $\beta$	~1.0	~1.2
IL-1 $\alpha$	~0.1	~0.1

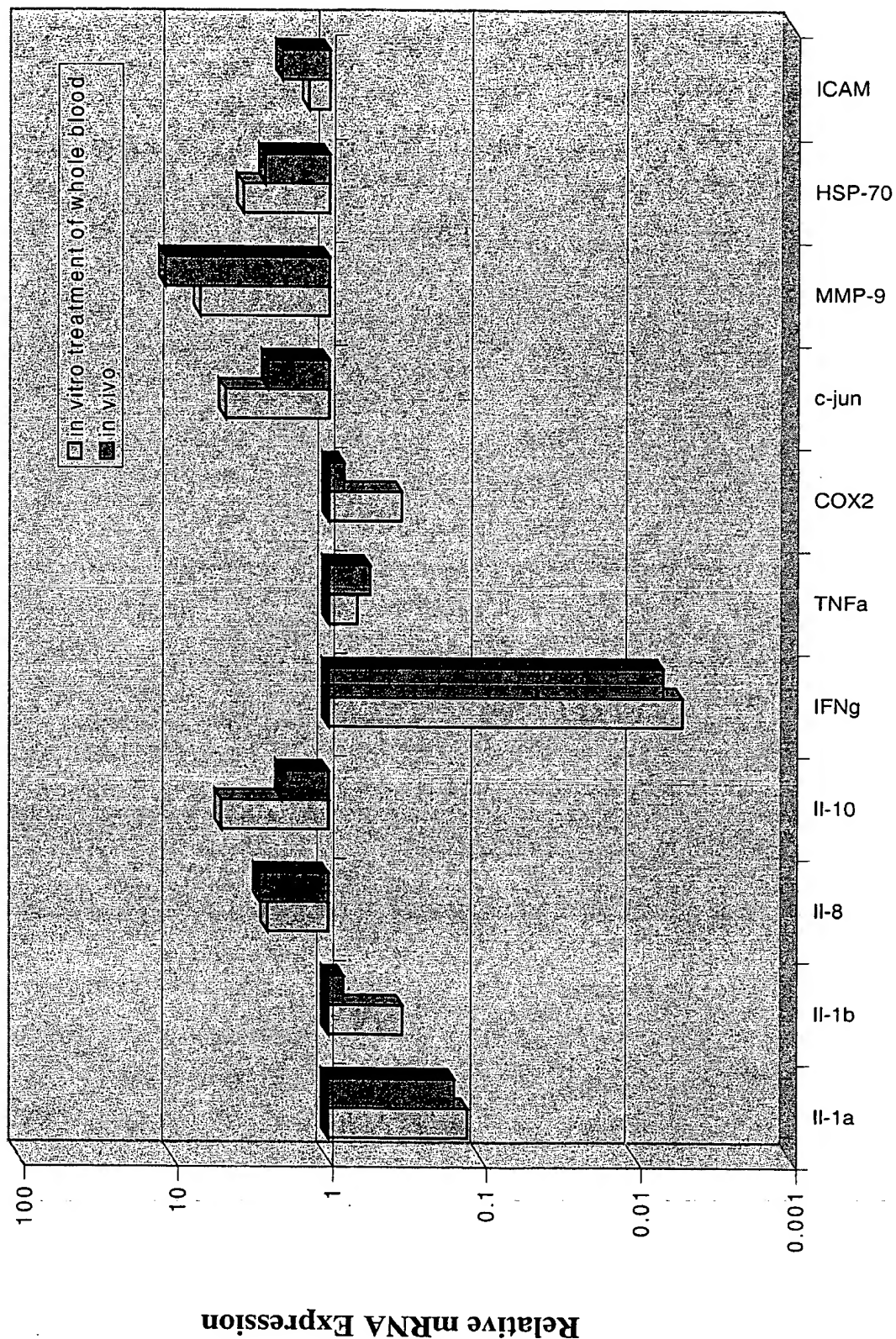
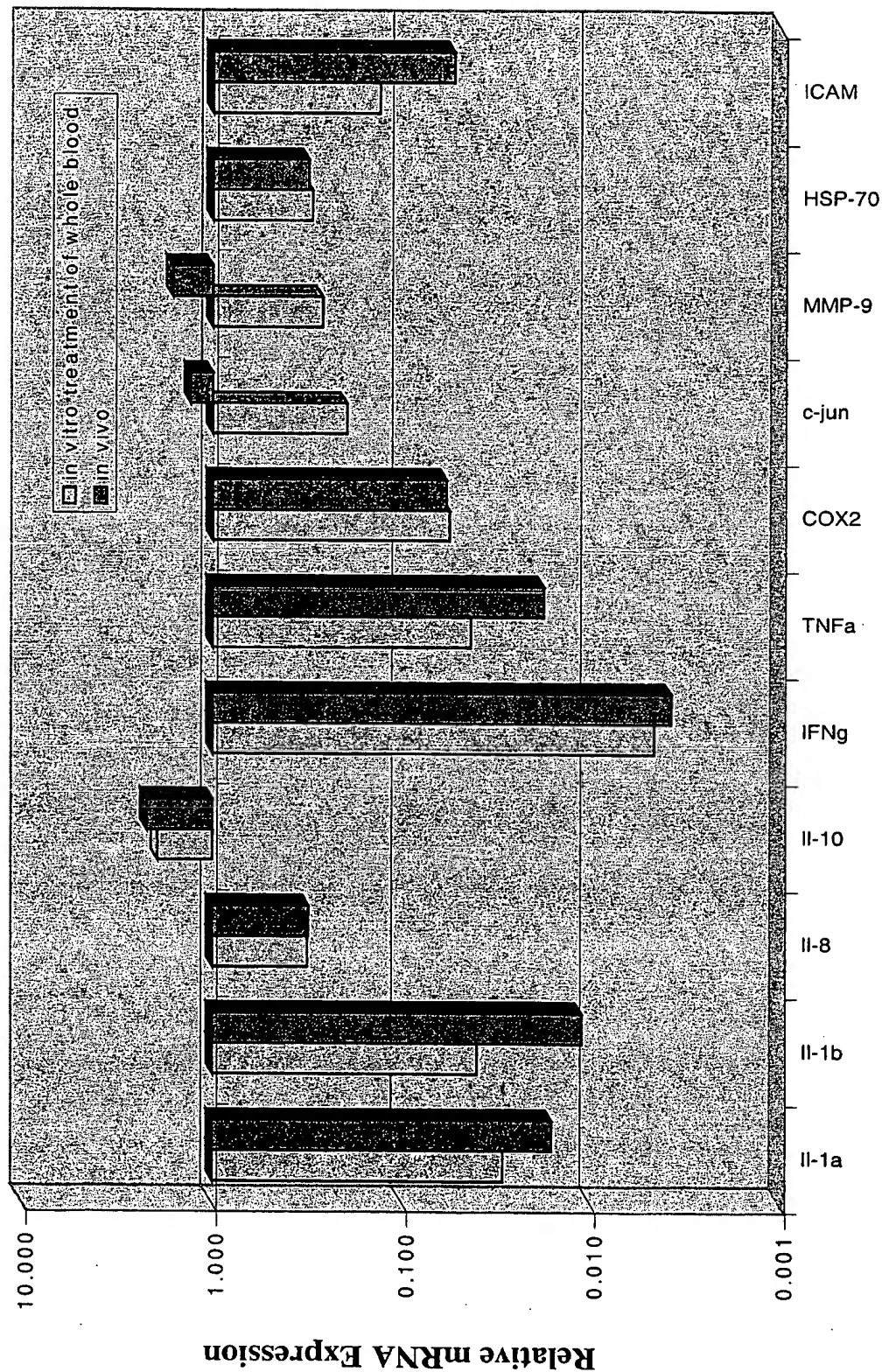


Figure 29(b). Comparison of Calibrated Profile Data Sets (Using Inflammation Precision Panel Subset)  
After In-vitro and In-vivo drug exposure (Steroids) -- Study 2

August 2000  
Subject 1JC



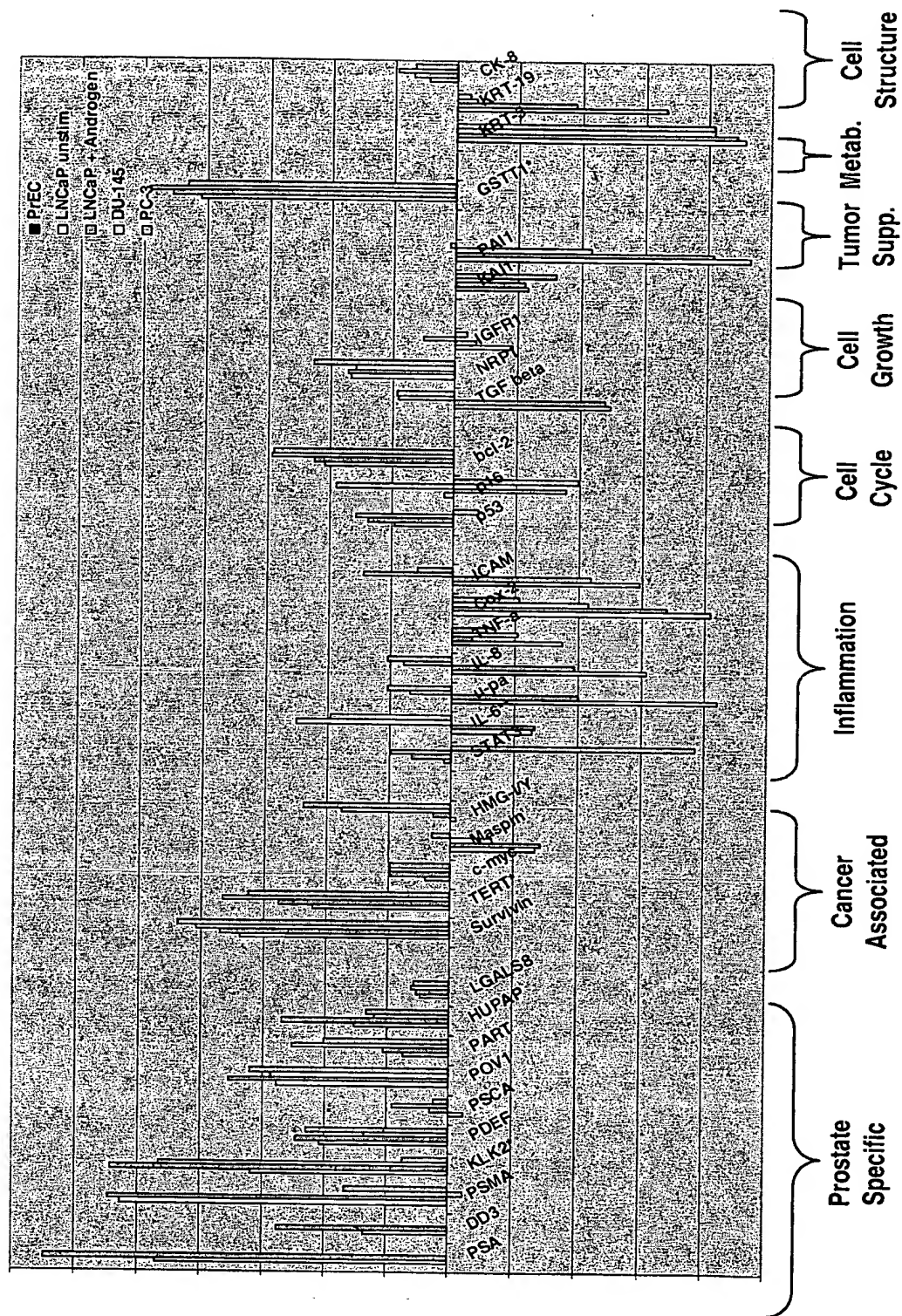




Fig. 31. Effect of the pharmaceutical clofibrate as measured on rat liver metabolism precision panel

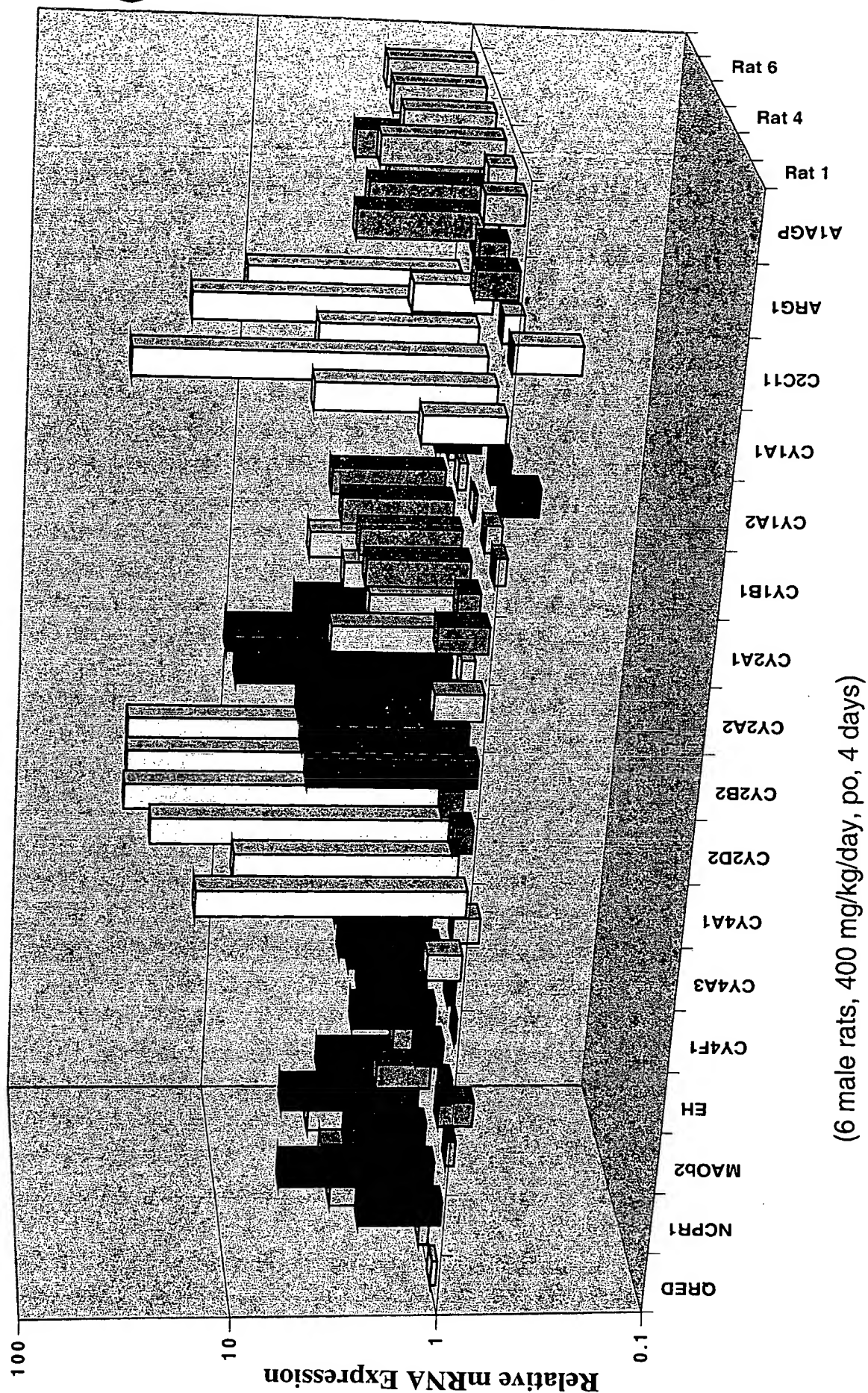


Fig. 32. A metabolism Precision Panel differentiates drug responses in rats.

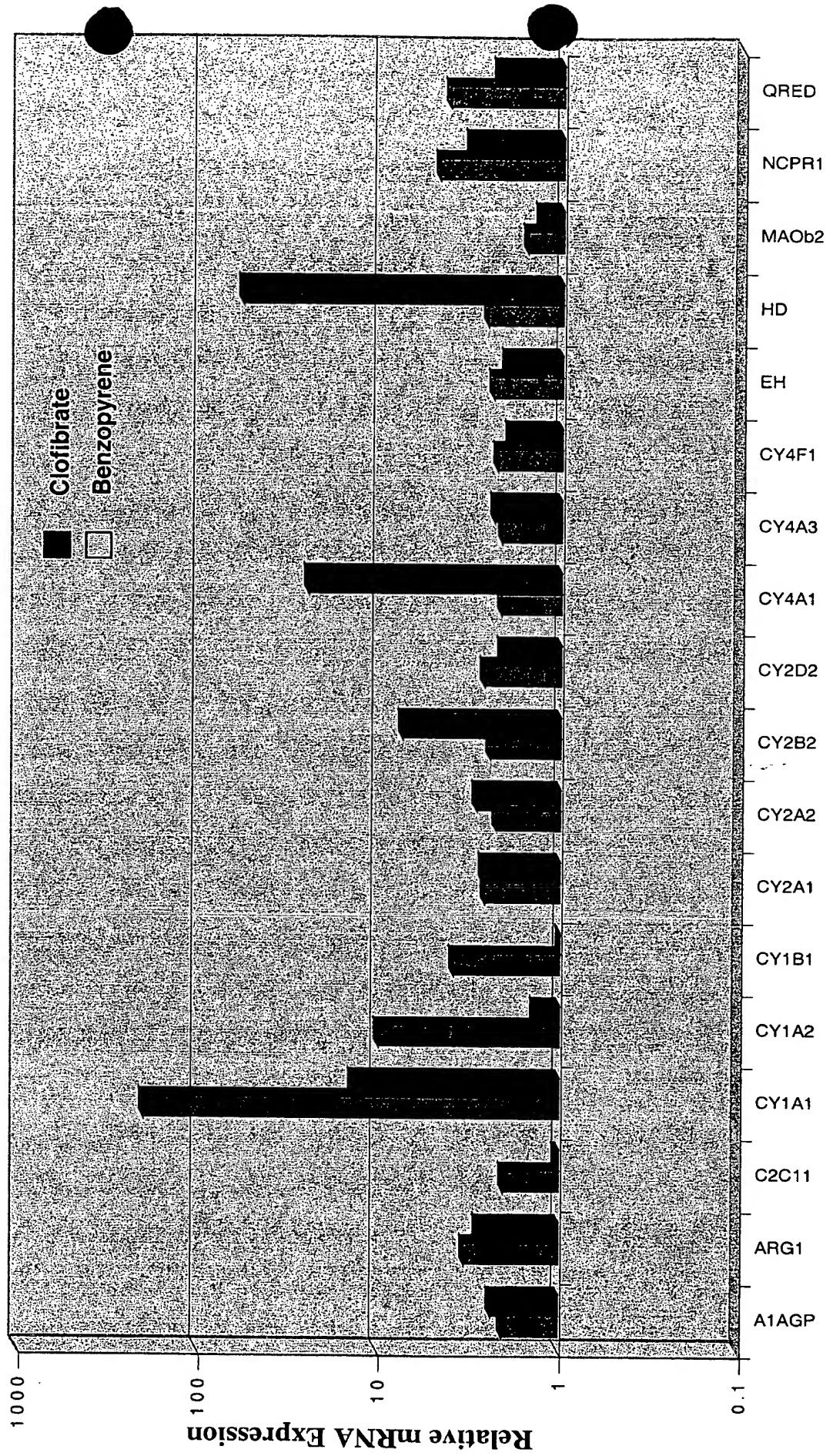
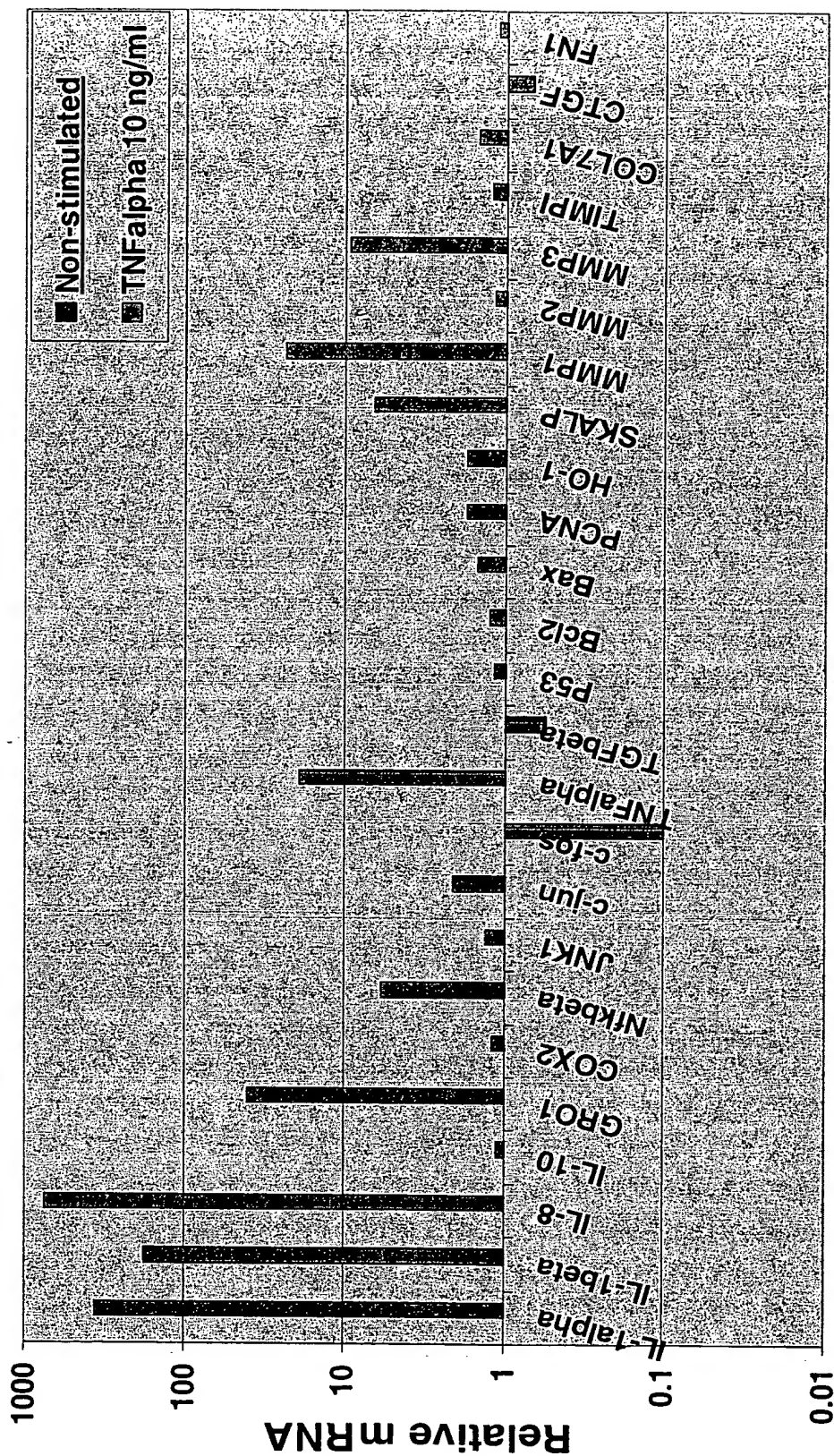


Fig. 33. A combination of the skin/epithelial and vascular precision panels show the effect of administration of a stimulant.



Skin Panel Genes



Figure 34: Example use of the human liver precision panel

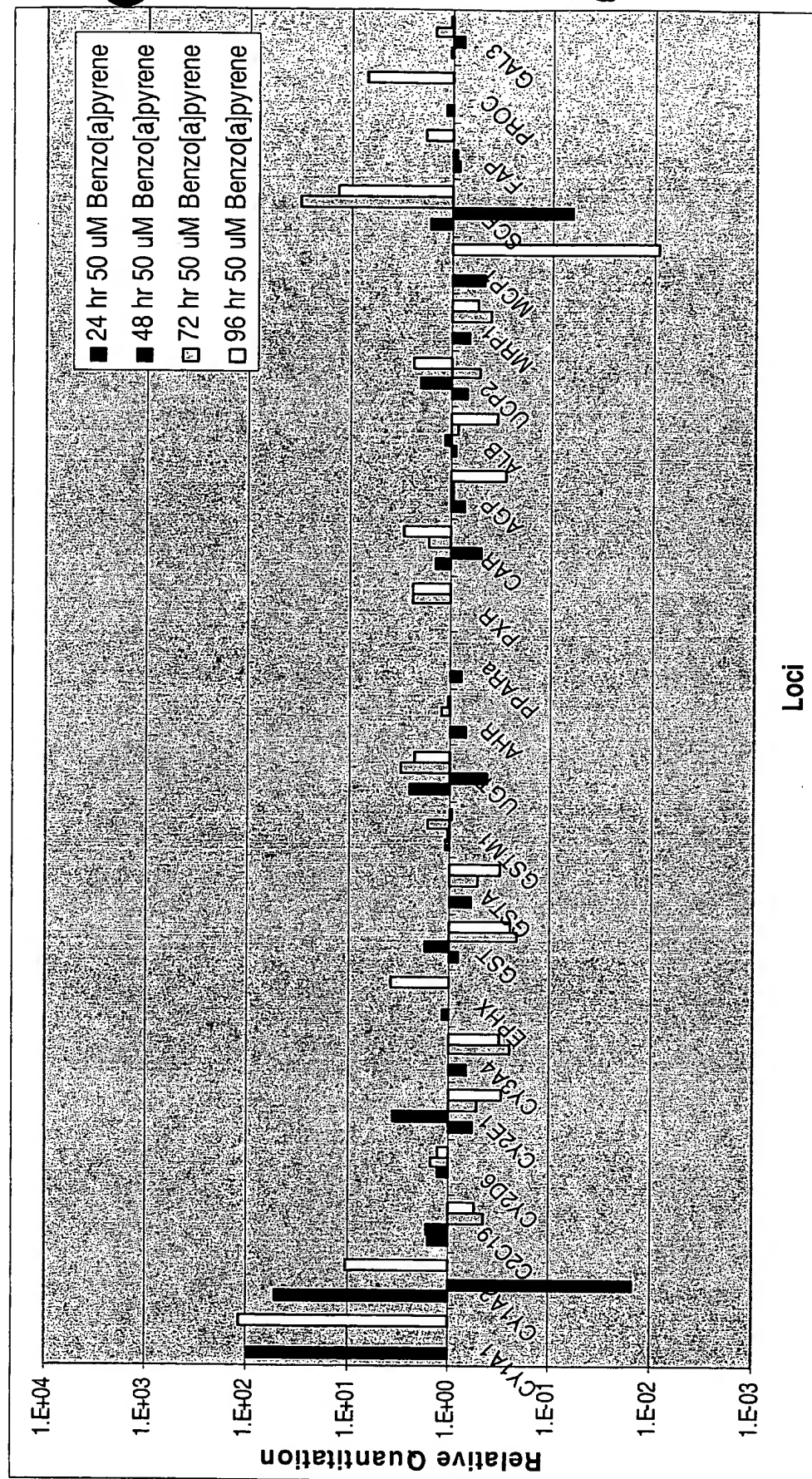


Figure 35. Human umbilical vein cells treated with TNF alpha and assayed on the vascular precision panel

HUVEC stimulated with TNF $\alpha$ , t = 24 hr

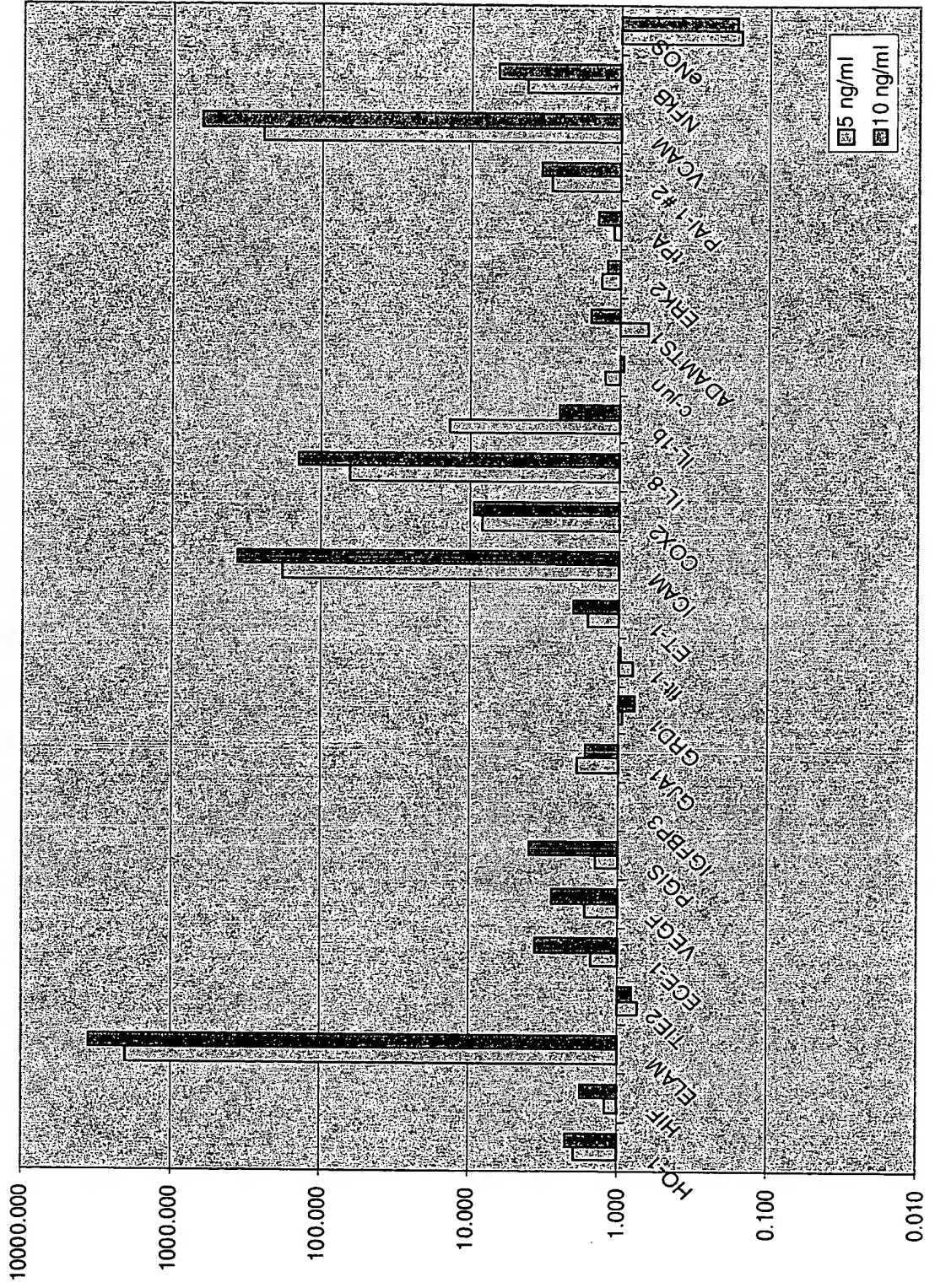




Figure 36. Assay of stimulated, human keratinocytes on the Skin Precision Panel

## Effects of N-acetylcysteine on UVB-stimulated Keratinocytes

